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DEPARTMENT OF REVIEWS

The Journal will make an especial feature of the review of monographs and books bearing upon the field of Internal Medicine. Authors and publishers wishing to subject such material for the purposes of review should send it to the editor. While obviously impossible to make extended reviews of all material, an acknowledgment of all matter sent will be made in the department of reviews.

Editor

ALFRED SCOTT WARTHIN, M.D.
Pathological Laboratory, University of Michigan
Ann Arbor, Michigan

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An Epidemic of Undulant Fever With a Study of the Associated Milk Supply

By MARIAN E. FARBAR, M.D., *College Physician, Richmond, Indiana*
and
FRANK P. MATHEWS, D.V.M., *Department of Veterinary Science, Purdue University Agricultural Experiment Station, Lafayette, Indiana*

BY no means a new, though as yet, an unsolved problem faces us in the seemingly sudden endemic appearance of undulant fever in this country. It is with the hope of aiding in the solution of its epidemiology and in the meantime to encourage a preventive campaign which would include as one of its objectives the control of the source of the infection that the present outbreak is brought to the attention of the Medical Profession.

The patients and their milk supply were circumscribed on a college campus, hence a study of both the patients and the herd was possible. The first two cases appeared early in January, 1928, and were diagnosed as "flu"; the third with a longer run of fever was suspicious of typhoid fever, and a Widal was conducted but with negative results; the fourth was so typical of remittent malaria that Wright stains were made but no plasmodia were found. The fifth case suggested tularemia on account of the prolonged illness with a high fever, a history of rabbit contact, and acute conjunctivitis. Acting upon this suggestion, a specimen of blood was sent to the Hygenic Laboratory, Washington, D. C., for a serological test, but a diagnosis of undulant fever was rendered by Dr. Edward Francis, whose timely assistance is hereby gratefully acknowledged.

A typical clinical syndrome of undulant fever was observed in twenty-five student patients and one laundress. A dizzy headache, malaise and nervousness, marked the onset of the disease and preceded by several days other distressing symptoms such as chills, fever, and a sweating which was frequently profuse. A low pulse rate, 40 to 110, rarely above, even with high fever was the rule. There was a mild leukopenia and an anemia present. All but four cases had two or more attacks of fever with apyrexia at intervals ranging from five days to two months. With the exception of these common symptoms, the usual wide variety of clinical manifestations which have been observed in other outbreaks, were noted. The accompanying fever charts illustrate the several types of the disease which were encountered.

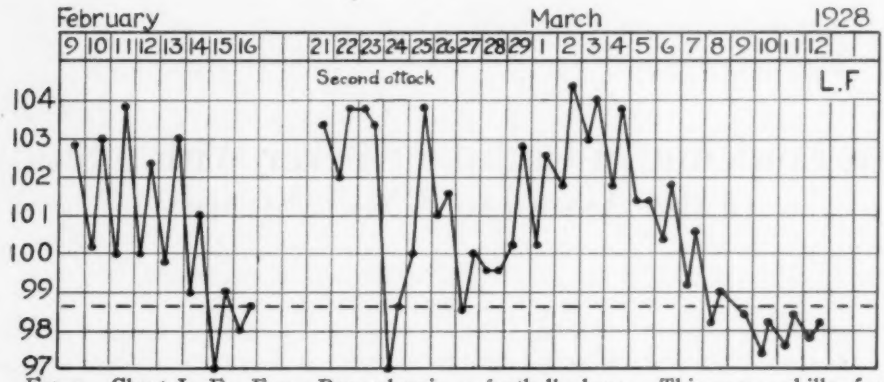

FIG. 1.—Chart L. F. From Pennsylvania, a football player. This was a chills, fever and sweating case with no outstanding symptoms otherwise. He is now apparently well and back on the squad.

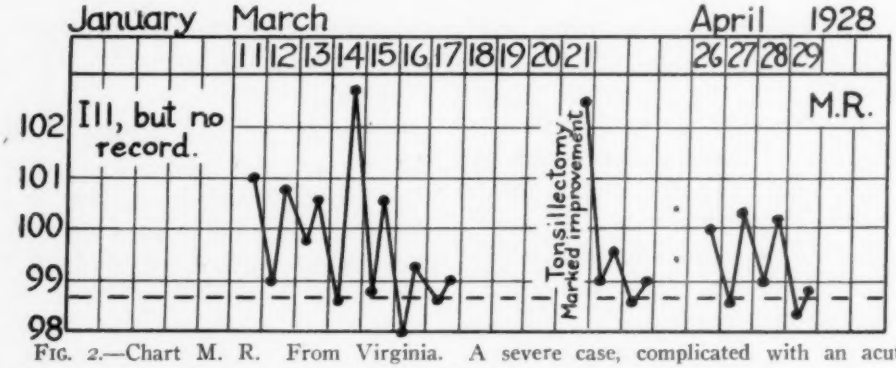

FIG. 2.—Chart M. R. From Virginia. A severe case, complicated with an acute exacerbation of a chronic tonsilitis; improved rapidly after tonsillectomy.

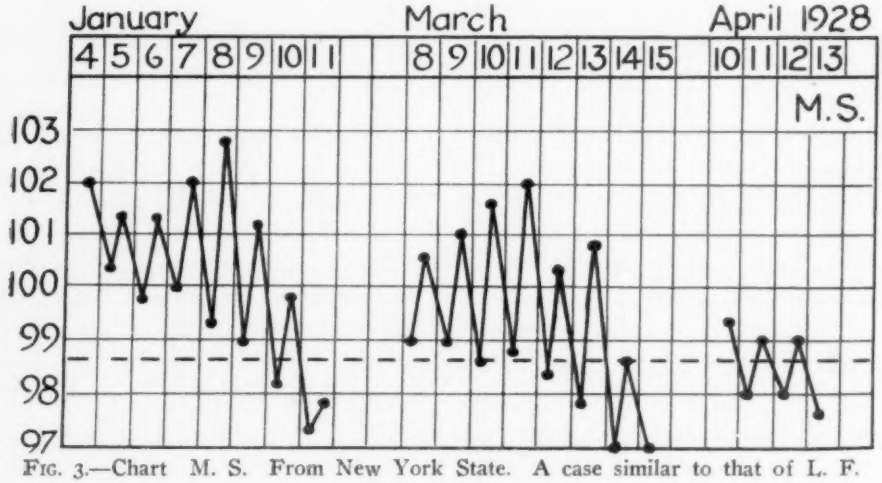

FIG. 3.—Chart M. S. From New York State. A case similar to that of L. F.

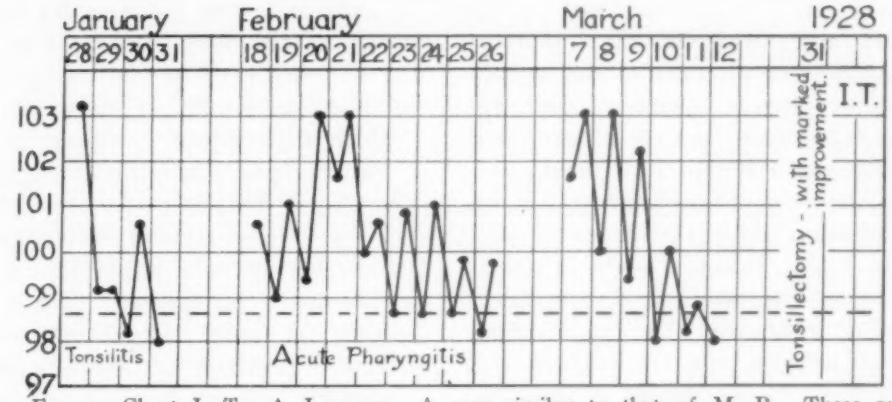

FIG. 4.—Chart I. T. A Japanese. A case similar to that of M. R. These and several similar cases suggest chronic infected tonsils as a factor in predisposing etiology.

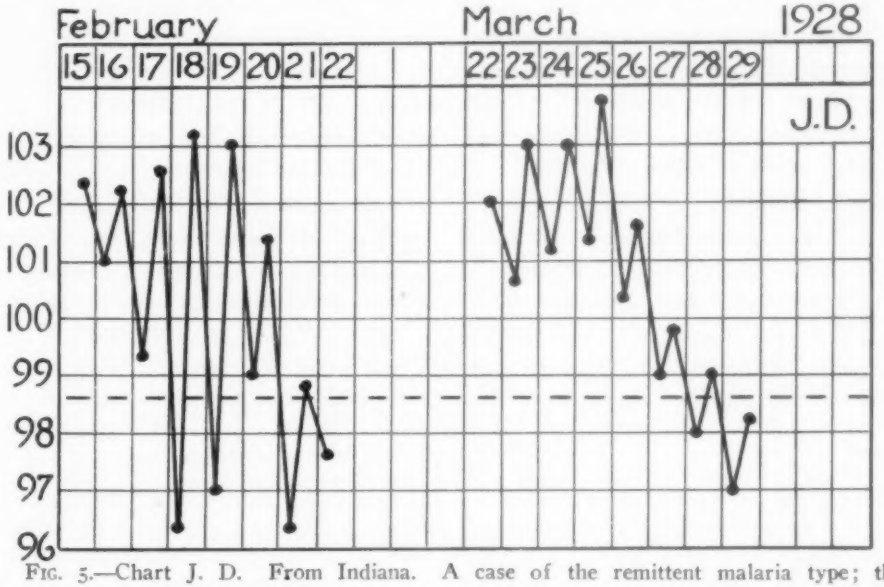

FIG. 5.—Chart J. D. From Indiana. A case of the remittent malaria type; the fever would remit each afternoon with a severe chill, preceding and a heavy perspiration following. The patient was quite ill but has apparently recovered at this writing.

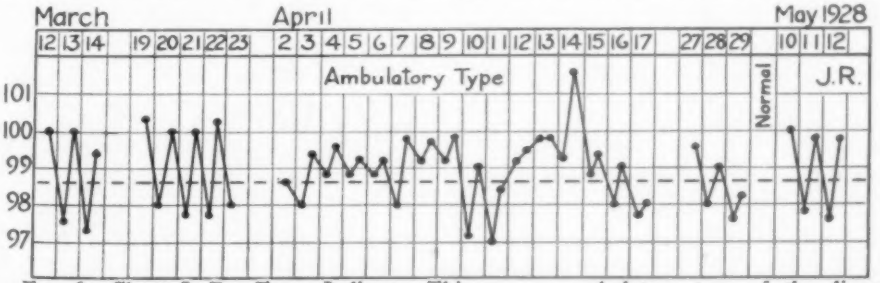

FIG. 6.—Chart J. R. From Indiana. This was an ambulatory type of the disease. This and two other cases continue to have undulations of fever every two or three weeks with sweating, chills and nervousness.

Of the twenty-six cases which were recognized clinically, fourteen gave positive reactions to the agglutination test for undulant fever, six were negative (one test only) and blood was not sent in from the remaining six. The macroscopic agglutination test was employed throughout. Dr. Francis used the three antigens, Br. abortus, Br. melitensis and B. tularense. The junior author employed but the one antigen, Br. abortus. The agglutinin titres of the fourteen positive cases are given in Table 1. It is of interest to note that the titres in fifty per cent of the tests were higher for Br. abortus than they were for Br. melitensis. Cross agglutination for B. tularense was slight, but observed in five cases.

In addition to the serological tests, the blood samples from the suspected cases were subjected to bacteriological examinations. Portions of the blood clots, and the serum not used for the serological tests were introduced into recently boiled bouillon and incubated under aerobic conditions and in jars in which approximately ten per cent of the atmosphere had been replaced with CO_2. For a period of one week daily transfers were made from the bouillon to agar slants but Br. abortus was never isolated. The remainder of each blood clot was macerated in sterile salt solution and injected into guinea pigs. The guinea pigs were killed six to eight weeks later and were examined for the lesions, and the presence of Br. abortus but with negative results in all cases. The blood of the guinea pigs never reacted to the agglutination test for infectious abortion.

The status of the dairy herd from which the entire milk supply was obtained was as follows: Twenty-three cows, seven of which gave positive re-

TABLE 1—AGGLUTININ TITRES OF FOURTEEN CASES OF UNDULANT FEVER

Case No.	Initials	Sex	Age	Date tested 1928	Brucella abortus No. 456	Brucella Melitensis No. 428	Bacterium Tularense	Treatment of Serum
1	L.F.	M	22	Mar. 24	1280	320	80	56° C. ½ hr.
2	M.R.	F	19	"	1280	1280	20	" "
3	M.S.	M	19	"	2560	1280	0	" "
4	I.T.	M		"	640	640	40	" "
5	J.D.	M	24	"	2560	640	160	" "
6	J.R.	M		"	160	80	0	" "
7	D.W.	M	18	Apr. 7	640	640	0	" "
8	A.C.	F	19	" 13	320	160	0	" "
9	O.R.	M	25	" 14	640	640	0	" "
10	W.O.	M	21	" 16	2560	1280	80	Unheated no preservative
11	E.J.	F	21	" 20	160	80	0	" "
12	S.R.	F	17	" 20	160	160	0	" "
13	M.C.	F		" 21	320	320	0	" "
*14	A.M.	F	47	May 22	100	...	.	" "

*Tested by the junior author, the other thirteen cases were tested by Dr. Francis.

actions to the agglutination test for infectious abortion. Br. abortus was isolated from the milk of three reactors, two of which were found to have advanced cases of mastitis. The udder of a third, reacting cow was likewise affected, although Br. abortus was not isolated from the milk of this animal. The cows had never been in contact with goats, and there were no hogs maintained upon the premises for breeding purposes. Adjacent to the cow lot was a pen of feeder pigs which had been placed in the feed lot as young pigs and were not of breeding age when the outbreak of undulant fever occurred.

About two months after the dairy herd was examined and corrective measures established, six of the gilts were isolated from the remainder of the pigs in the feed lot. The milk from the mastitis cases was then fed to the six gilts for a period of two weeks. (Bacteriological examination showed that two of the cows were still eliminating Br. abortus in the milk). Immediately following the feeding period four of the gilts were bred. The six animals have been repeatedly tested with the agglutination test for infectious abortion, but with negative results to date. One of the gilts had evidently conceived before the male pigs in the feed lot were castrated, since this animal gave birth to seven live pigs, nine weeks after she was segregated with the other five gilts. The pigs were killed as soon as they were farrowed and their organs examined for the presence of Br. abortus but with negative results. Negative results were likewise obtained with the fetal membranes.

Discussion

Since there was no history of contact with goats or aborting hogs, it is quite improbable that these animals had any direct connection with the present outbreak of undulant fever. That the infected dairy herd was directly responsible was supported by several important facts; first, the demonstration of Br. abortus in the milk; second, all the undulant fever cases were heavy consumers of raw milk, with two exceptions, and in these two cases cream was consumed with cereals; third, since pasteurization of milk was established no new cases have developed; fourth, the sudden outbreak among students which had assembled from a wide range of territory indicated that the infection was acquired locally and not imported.

A point of interest in the present observations is the number of clinical cases which failed to react to the agglutination test. Similar observations have been made by other investigators and serve to illustrate the fact that a single negative agglutination test is insufficient evidence to exclude undulant fever, in the face of a typical clinical syndrome of the disease. It would have been of scientific interest to have been able to isolate Br. abortus from the blood-stream of some of these patients, but since this was not accomplished, the results should be interpreted as an absence of bacteremia and not as the absence of Br. abortus as the etiological factor.

The tendency of some investigators to consider swine as the reservoir of infection is not supported by the present observations. The failure to

infect gilts by feeding milk which was shown to contain B. abortus must be considered as evidence that the organism concerned in this instance was not the porcine type. Furthermore, the cultures of Br. abortus which were isolated from the milk have been found by both the junior author and Dr. I. F. Huddleson,* to be of bovine type.

*Personal communication.

Report of a Case of Primary Multiple Myeloma With Bence-Jones Protein in the Pleural Effusion

By Eugene E. Marcovici, M.D., F.A.C.P., *New York City*

J. H. CORIAT in 1903 described for the first time the occurrence of Bence Jones protein in the pleuritic effusion of a patient suffering from Korsakoff's psychosis, with extreme tenderness of the ribs and no albumosuria.

The case I wish to report has been under my observation from Dec. 13th, 1927, till to its exitus on April 13th, 1928. The history presents the following data: Mrs. Th. B., 55 y. old, born in Fubine, Italy. Mother died at the age of 40 due to some form of anemia. Father died at the age of 70, after apoplexy. One sister 60, a brother 65, both well. Patient menstruated at the age of 14, married at 18, had six children, all well. Her husband died at the age of 40 from Bright's disease.

Patient's normal weight was about 100 lbs., had worked very hard and was poorly nourished. Outside of constipation, the patient did not remember any serious ailment.

In February 1927, the patient felt neuralgia-like pains over the left side of the chest, most of the ribs were sensitive at the slightest pressure. No fever, appetite poor.

In April she went to the farm of her brother in Connecticut for a rest; while carrying a pail of water, she felt a sudden pain in the left side of the chest, similar to the breaking of some ribs. In August 1927 the patient came back to the city. The pains were rather increased, severe shooting pains in most of the ribs, on the left side and over the heart region. No appetite, always constipated. Loss of weight of about 12 lbs., sleep very poor.

In October 1927, the patient had X-rays taken of her chest, report not known to the family. In November at the Reconstruction Hospital, where I saw the patient in consultation, they were of the opinion that primary carcinoma of the cecum was the probable diagnosis and that the rib conditions were carcinoma metastases. I found then no signs of malignancy in the intestinal tract.

On December 13th the family brought the patient to my office for another examination and further treatment.

She complained of severe pains in the left side of the chest, poor sleep on account of the pain, sometimes night sweats, seldom cough. Walking was difficult, weakness, lack of appetite, gradual loss of weight, constipation, no nausea. Shortness of breath, sporadic pains, redness and slight swelling of the right toe and the right trochanter. Headaches mostly forehead, no dizziness. Paresthesia in both forearms. Pt. was pale, prematurely aged, and poorly nourished, weight 89 lbs., Temp. 99.6°, Resp. 36, Pulse tachycard. 104, Blood pressure 110/80. Dyspnea. Blood examination: E. 4475000. L. 13150. Hemoglobin 85%. Differential leucocyte count: P. 72, L. 3, l 11, E. 2, Ba. 2, n. Mye. 10. Urine examination: Albumin in traces, Sugar neg., Bence Jones protein neg. Sediment: no casts, few epithelial cells and W.B.C. The head was carried inclined toward the left, the muscles of the neck were contracted (not a recent condition), possibly following

a rheumatic myositis. The face was wrinkled, pale, emaciated. Panniculus adiposus was absent. The head nerves were normal. The tongue was not coated, slightly dry. The neck organs were normal. Pharynx and larynx did not show any peculiarities. No gland enlargements, the veins were not distended. The chest looked very narrow, the breathing appeared superficial and frequent.

The lower intercostal spaces showed retraction during inspiration, the right side of the thorax expanding less than the left; basal adhesion left, dulness over the right lower lobe. Both apices retracted. There was vesicular breathing over the apices, no râles; over the right base were friction sounds; over the left lower lobe reduced breathing sounds, no râles or friction.

The fluoroscopic examination of the chest, showed that several ribs have undergone a destructive process, especially the fifth right rib and the third, fourth and fifth left rib. The right hilus showed a great amount of infiltration, in the shape of an interlobar effusion. The right base showed adhesions. The heart of normal size, the sounds clear, the pulse rhythmical, equal but rapid.

The examination and palpation of the abdomen did not show any pathology. The diagnosis made at my office was multiple myeloma of the ribs and advised that the patient be placed in the hospital for observation.

The patient has been under very careful observation. The temperature had been normal up to the time of her admission, when it reached 101.6 F. Upon examination I found an accumulation of right pleural effusion. The X-ray examination by Dr. Pound on January 9 reports the following findings: Films were made of the skull, forearms, femurs, legs and feet. There was no evidence of any pathological changes in the bones or the periosteum. Films of the colon after a barium enema showed no evidence of cancer or obstructive loops or kinks. Film of the chest showed the lower half or two thirds of the right chest filled with a pleural effusion. The fifth left rib showed complete destruction of all of the bony portion except the extreme anterior end. The sixth rib left posterior axillary line showed a destruction for a distance of a trifle over an inch. The seventh rib posteriorly showed several small punched-out areas. The tenth rib left showed destruction of the posterior two thirds. There were a few areas of pleural involvement in the left chest (Fig. 1). Diagnosis: Multiple myeloma.

On January 9, the temp. was 101.6 F. The urine was negative for Bence Jones; the blood count findings were as follows: E. 450,000. L. 15100. Hem. 100%, P. 85, L. 12, E 1. The pleural effusion reached the spina scapulae. The fluid obtained through paracentesis had a specific gravity of 1024, the reaction for Bence Jones protein was doubtful (Wells, Chem. Path., W. B. Saunders. Phila. 1925, p. 597). The X-ray report (Dr. Pound) on the day after the paracentesis, Jan. 10, read: Pleural effusion has been removed through tapping. Considerable amount of fluid has been removed. The sixth rib on the right side in the axillary line showed a destruction for a distance of an inch and a half (Fig. 2, Fig. 2a).

The blood count on Jan. 10th was L. 15000. P. 81, L. 5, E. 1, l 7, Ba. 2, n. Mye. 4.

On Jan. 11th: L. 10,000, P. 77½%, L. 6, l 7½%, Mo. 1, Trans. 0.5%, E. 1, Ba. 1%, Myel. 1½%.

On Jan. 14th the temp. was 99.9°, the leukocyte count 8200, P. 73, L. 12, l. 3, Mo. 2, E. 4, Ba. 2, Mye. 4.

On Jan. 18th, leukocyte count was 8000. P. 68, L. 7, 1.8, Mo. 7, Trans. 3, E. 1.5%, Ba. 1.5%, Myel. 2.

On Jan. 21st, L. 10,000, P. 73, L. 11, 1.5, Mo. 4, E. 4, Ba. 1, Myel. 2. The fluid in the chest had collected again. The X-ray report as follows: Effusion in the right chest has reaccumulated. There appeared to be a number of punched-out areas in several of the ribs, which showed no previous involvement. The sixth rib showed further destruction in the posterior portion (Fig. 3).

On Feb. 8th the X-ray report reads: Pleural effusion filling most of the right chest; several small areas of pleural thickening (Fig. 4). Blood report: Hem. 80%, E. 5,000,000, L. 8000, P. 69, L. 1, 1.26, Mo. 2, E. 2.

FIG. 1

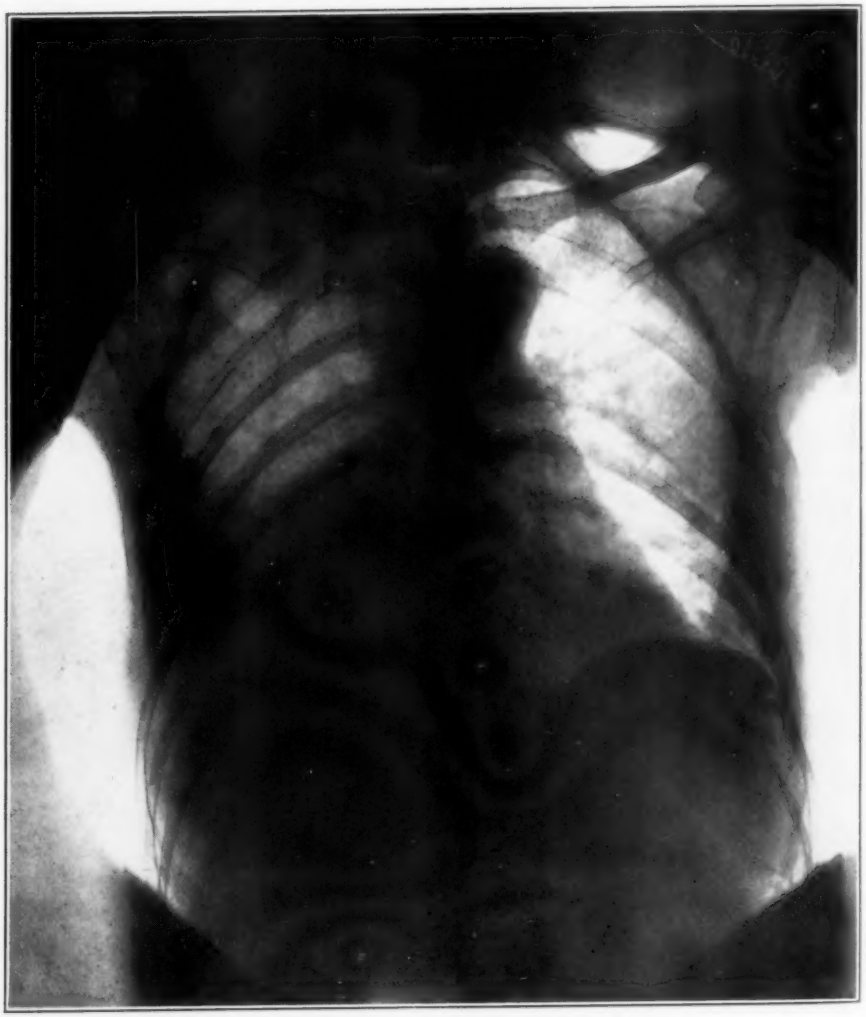

FIG. 2

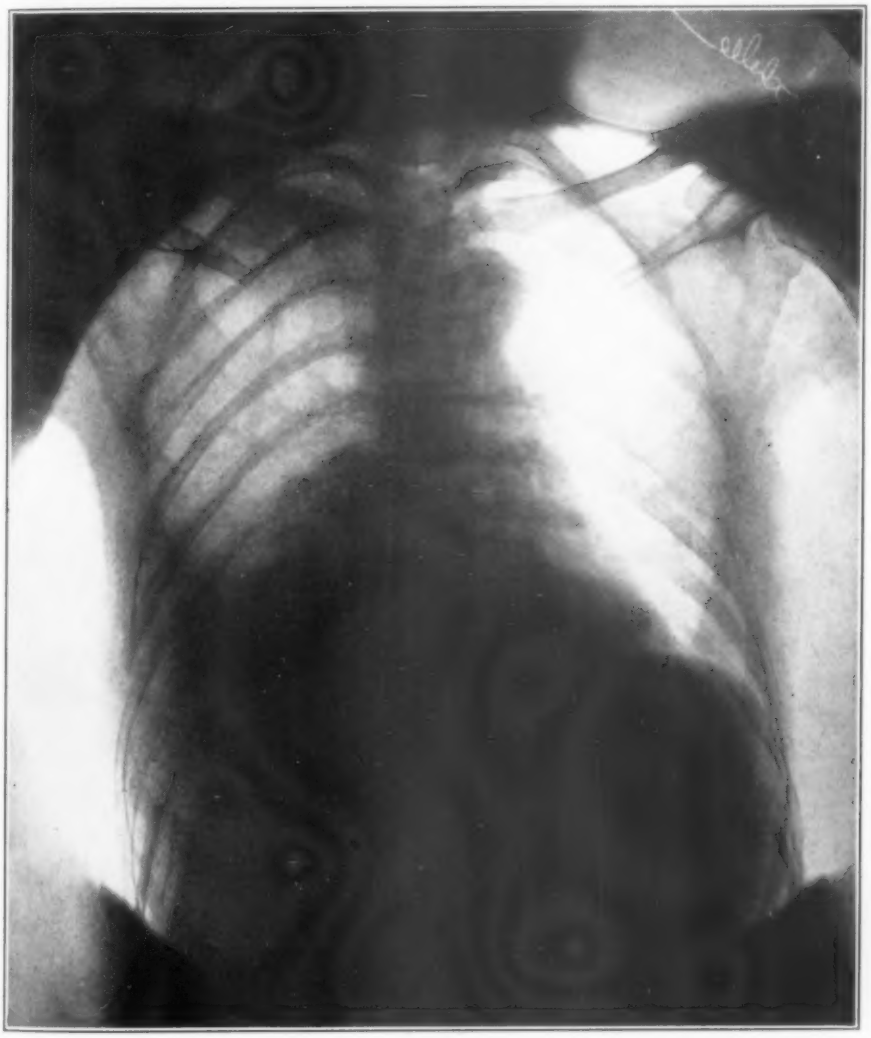

FIG. 2a

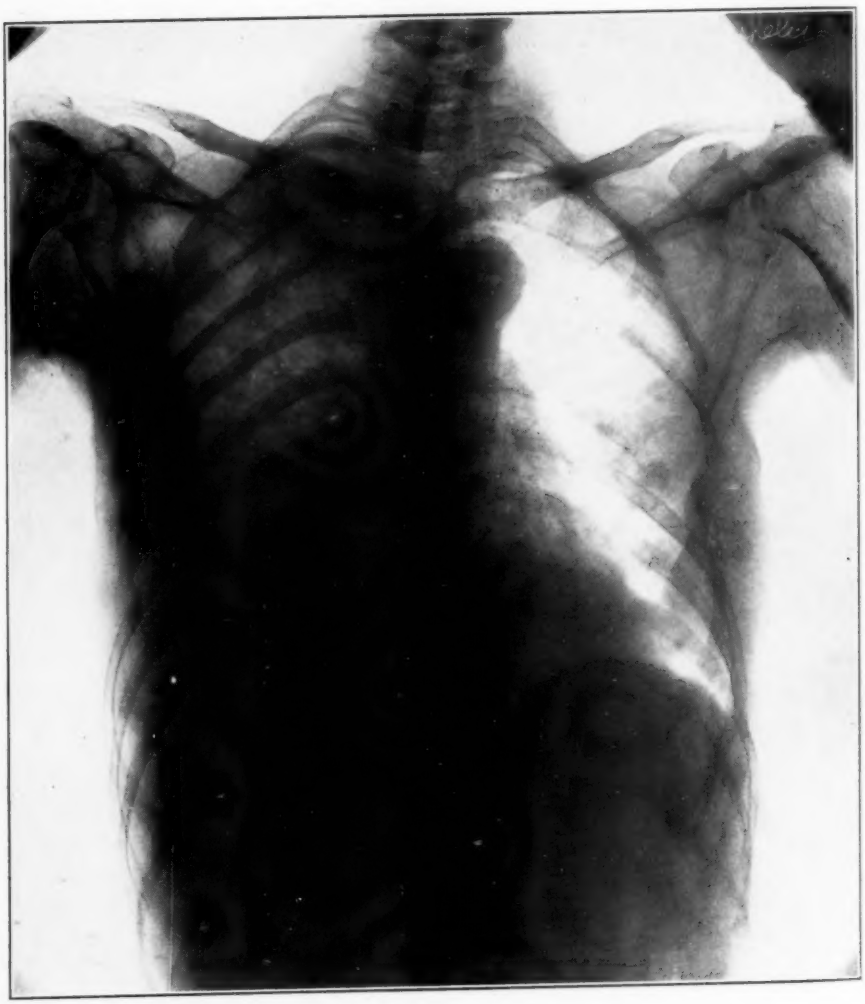

FIG. 3

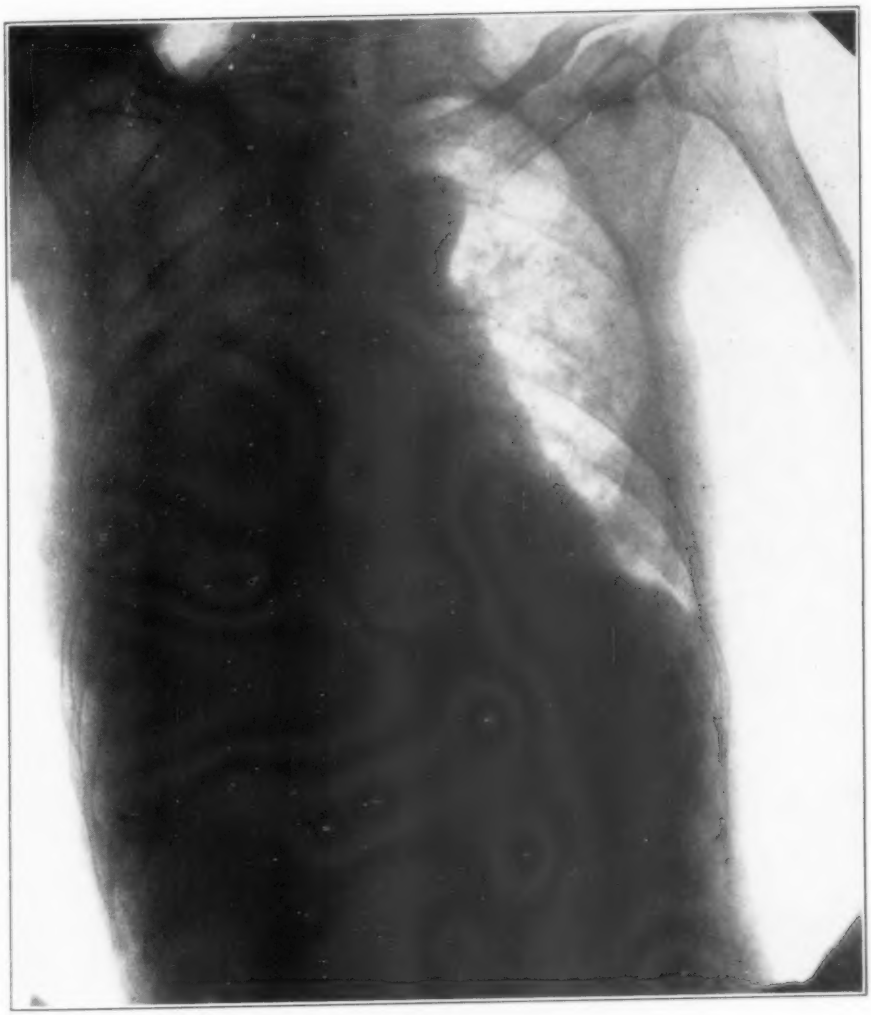

FIG. 4

On Feb. 10th through paracentesis 1200 cc. of fluid was removed, the specific gravity was 1024. *The Bence Jones reaction was positive* (Dr. Killian).

On Feb. 14th the blood report was: Hem. 94%, E. 4,500,000, L. 5000, P. 71, L. and 1.25, Mo. 2, Bas. 1, E. 1. The blood chemistry: Urea N. 17.1, uric acid 1.5, sugar 68 mgr.

On Feb. 21st, 1928, the X-ray report says: more pleural involvement in the right chest with further destruction of the ribs previously noted. The fourth and sixth ribs on the left side showed an increased destruction (Fig. 5).

On Feb. 26th, patient complained of pains in the lower ribs on both sides. The examination proved both fifth ribs very sensitive to touch. The cachexia is progressing rapidly. Still the blood report does not show any anemia: Haem. 85, E. 5,500,000, L. 7100, P. 74%, L. and l. 19%, Mo. 3%, E. 4%.

While the patient used to move around her room, and sometimes sit for few hours in a chair, she now keeps quietly in bed, avoiding any other position than the one of lying flat on her back.

On March 2nd, I made a more thorough inquiry about her condition and a renewed complete examination. The complaints were: a shortness of breath which is less intensive when the pains are localized in the upper back (shoulder and shoulder blades) than when they involve the lower right ribs. A certain catching of the breath, corresponding to the lower left ribs, is always present, whereas at the beginning of the disease, was only of short duration. No appetite, nausea quite frequently. Constipation, but no pains in the abdomen, unless after a laxative. There is no burning passing the water but she has to void often. No cough, sleep very poor, unless with the help of hypnotics. Patient complains also of a tired feeling in the arms, more so than in the legs. The motion in the arms gives pains in the chest. The speech is quite difficult, partly through shortness of breath. Walking is very difficult, with increased dyspnea and choking feeling. While sitting in a chair the patient has pains in both lower parts of the chest, left more than the right; the right trochanter is also painful (the mentioned spots and sometimes the right and left big toe would become very painful for a short period of time, showing redness on the surface and a certain amount of swelling, like in gouty attacks, and then disappear, with no X-ray findings). There is a numbness in both arms. Examination shows: temp. 98.8°, blood pressure 110/80, pulse 104. Patient is sitting in a chair, appearance cachectic, dyspnea, frequency 36. The inspection of the chest shows great emaciation, the scaleni and pectoralis muscles pulled strenuously with every breath, the intercostal spaces show inspiratory depressions. The whole chest very sensitive to touch, especially the lower ribs, the lower part of the sternum, the processi spinosi of the 1st, 2nd, and 3rd dorsal vertebrae. The percussion gives dulness from the upper margin of the third right rib and from the middle of the scapula down. Compression breathing to be heard over the third and fourth intercostal spaces, no breathing sound or vocal fremitus over the dull part of the right chest. The left lung base adherent from a previous basal pleurisy, the breathing sounds over the left lung negative. The heart action is very fast, no murmurs, no arrhythmia. The abdomen meteoric, due more to the opiates the patient gets in order to obtain some sleep, than to any other source. The paresthesia of both arms, left more than the right, is very pronounced.

On March 6th the fluid in the right chest has reached anteriorly the lower margin of the right second rib and the spina scapulae posteriorly. Through renewed tapping of the pleural cavity 800 cc. of fluid was obtained. Blood was taken the same day for the detection of Bence Jones protein in the serum. Report on Bence Jones protein (Dr. Killian) was: positive in the chest fluid, faintly positive for the blood serum.

X-ray examination on March 7th reports: pleural effusion still present in the lower right chest. Advanced destruction areas in the left ribs; sixth rib on the right side shows increased destruction (Fig. 6).

Blood examination report: Hem. 96%,

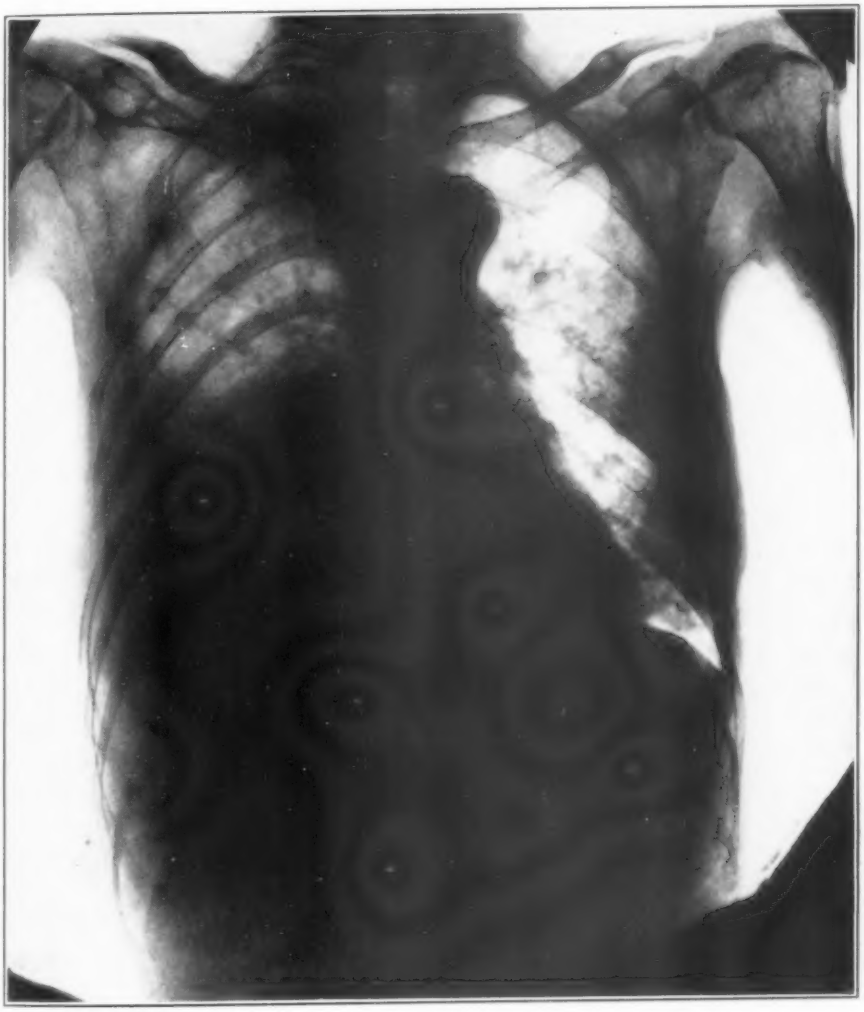

FIG. 5

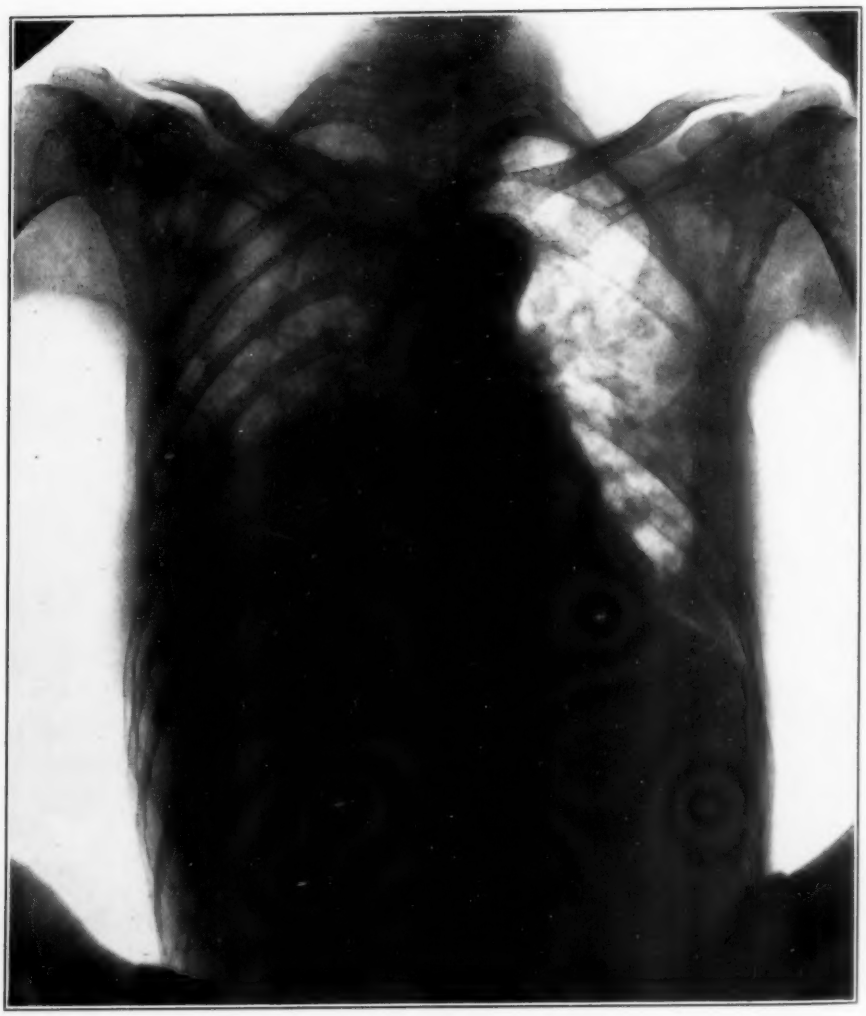

FIG. 6

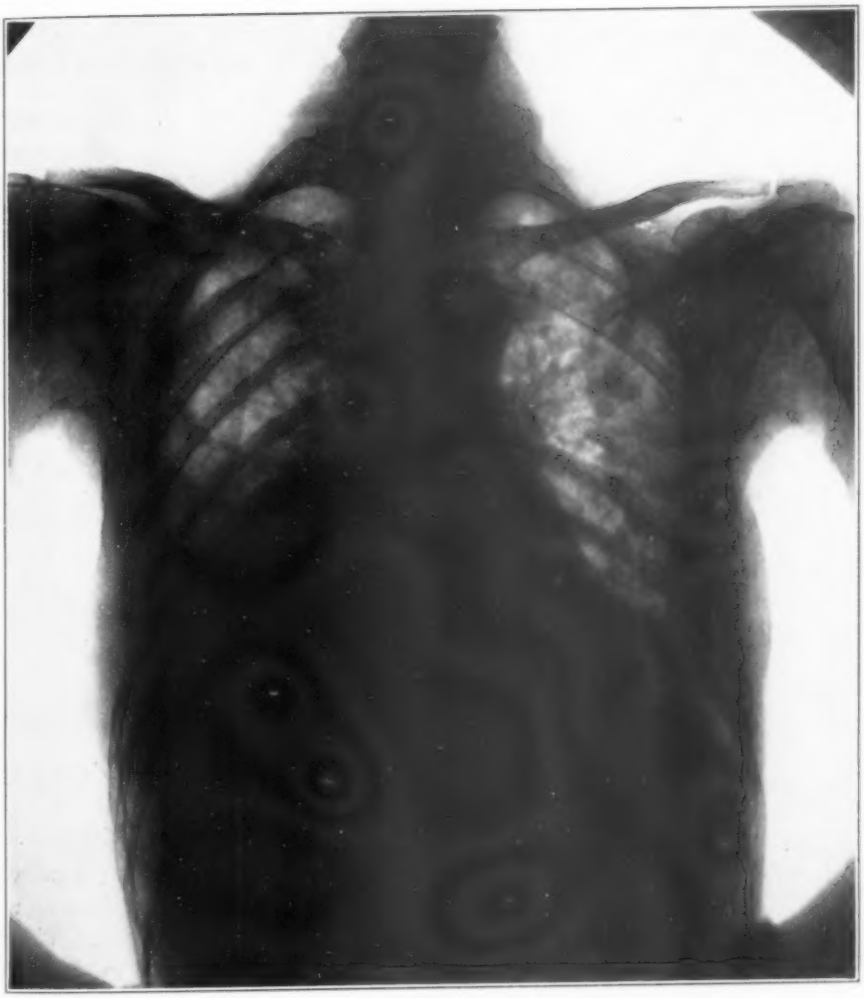

FIG. 7

E. 5,000,000, Leukocytes 7800, P. 63, L and l. 32, Mo. 4, E. 1. On March 23rd: Hem. 85%, E. 5,000,000, L. 12,000, P. 78, L and l. 17, Mo. 2, E. 2, Ba. 1.

March 25th the dyspnea is increasing, excessive pains in the lower left ribs, pt. very restless, morphine needed every night to induce some sleep.

On March 26th another paracentesis was performed, 800 cc. of fluid was obtained. The dulness decreased to the upper margin of the sixth right rib anteriorly, and to the angulus scapulae posteriorly. Breathing was easier. Temperature normal, Pulse 120. Blood was also taken and the bloodserum showed a positive reaction for Bence Jones protein, as did the pleural fluid. The urine of the same day, for the first time since the beginning of the observation, was positive for Bence Jones protein, 2.91%. The X-ray report, from pictures taken after the removal of the fluid on March 26th, reads: Pleural effusion remaining in the right chest. There is a mass around the right root about the size of an egg, which has been present throughout the series but shows more definitely in the recent films; the fourth rib left shows more destruction and the sixth rib on the left side is practically destroyed. There are numerous changes throughout the chest (Fig. 7).

Diagnosis (Dr. Pound): Multiple Myeloma with progressive rib destruction; pleural and lung involvement.

The blood count on April 6th: Hem. 96%, 5,000,000; leukocytes 9100; P. 72%, L. and l. 27%, Mo. 1%.

The temperatures to April 12th were normal. The cachexia rapidly progressing, the pulse getting faster and irregular, the patient refuses any nourishment. The pains were so excessive that we had to keep her the last days under morphine. After a comatose stage of one day, the patient died on April 13th, 1928.

The post mortem was not possible, not having the consent of the family.

The therapeutic measures during the time of her illness were: roborantia, quartz light, camphor in oil and mirion, with no advantage. The deep X-ray therapy as one would suggest has not met with the approval of the specialist in the case, the conditions being too advanced. Intravenous Thorium X injections, which I would have liked to try, were not available. There is certainly for myeloma a more definite impossibility to reach any therapeutic success than in any other malignant tumor.

The differential diagnosis from secondary multiple myeloma was the absence of the primary tumor; from tuberculosis of the ribs with pleurisy, the absence of any tuberculous symptoms; from rachitis, osteomalacia, osteitis deformans, caries of the vertebrae, isolated vertebral tumors, the X-ray findings and the absence of the Bence Jones protein in the urine. Senile osteoporosis leads also to spontaneous fractures, the pains are not very intense. Chloroma has a leukemic blood picture, and the localization is mostly in the flat bones of the skull.

The most characteristic symptoms for myeloma are: Bence Jones protein in the urine, the cachexia, the spontaneous rib fractures and deformities and the intensive periodical pains, the X-ray findings, the recurrent fever, the absence of any too pronounced changes in the blood with the exception of the slight myelocytosis and the presence of basophiles (common occurrence in all malignant tumors).

Conclusions

The reported case of primary multiple myeloma presents certain peculiarities, which may be of interest.

The ribs alone were found affected, in none of the other bones were tumor formations detected. The destruction of the ribs led to the pleural effusion, not a common occurrence.

The pleural fluid contained Bence Jones protein.

The blood serum and the urine contained also Bence Jones protein, the urine only toward the end of the patient's life.

The X-ray examinations have helped to the early diagnosis, when

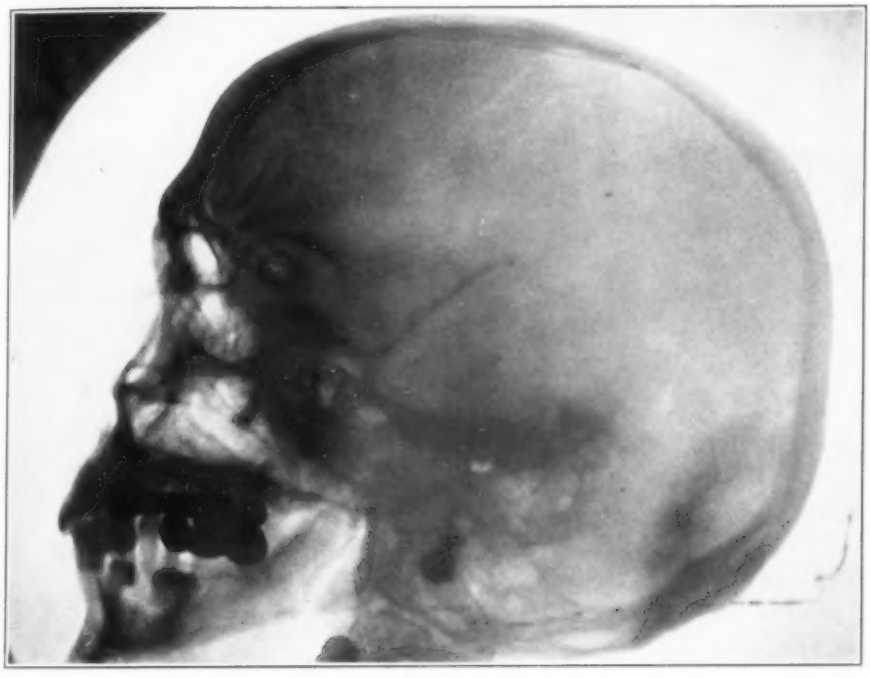

Fig. 8

the other symptoms were not evident as yet.

The hematological findings in this case were: Normal hemoglobin and red cell count, a normal leubocyte count in the fever free period, a slight leukocytosis with the accumulation of the pleural fluid. An increase in the percentage of the eosinophiles (to 5%), of the basophiles (to 4%), the appearance of neutrophile myelocytes (up to 6%); a polynuclear leukocytosis with the pleural complication.

The recurrent type of fever since the appearance of the lung complication.

The temporary pericostal inflammation over both trochanter and the big toes.

Paresthesia of the upper extremities.

The progressive cachexia.

The duration of the disease since the first symptoms, has been a little over one year. The early diagnosis by means of X-ray should be attempted in every suspicious case (some are taken for intercostal neuralgias) and deep X-ray therapy, radium or mesothorium irradiations tried from the beginn. Intravenous injections of Thorium X are supposed to be of value.

The therapeutic measures in this case were of no value. I have used quaetz light, arsenic and iron; mirion; sedatives and narcotics toward the end were unavoidable.

The multiple myeloma damages the bone marrow, the most important blood producing organ. While in some instances, the multiple myelomas

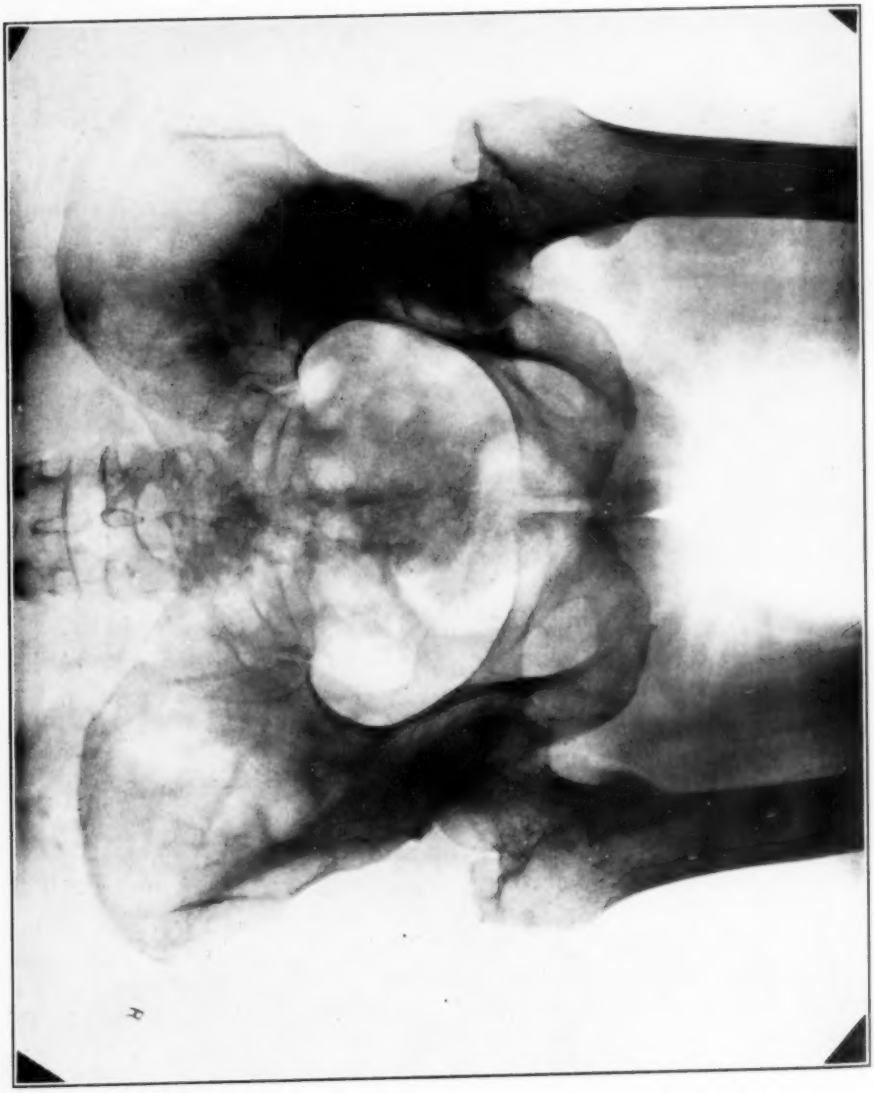

FIG. 9

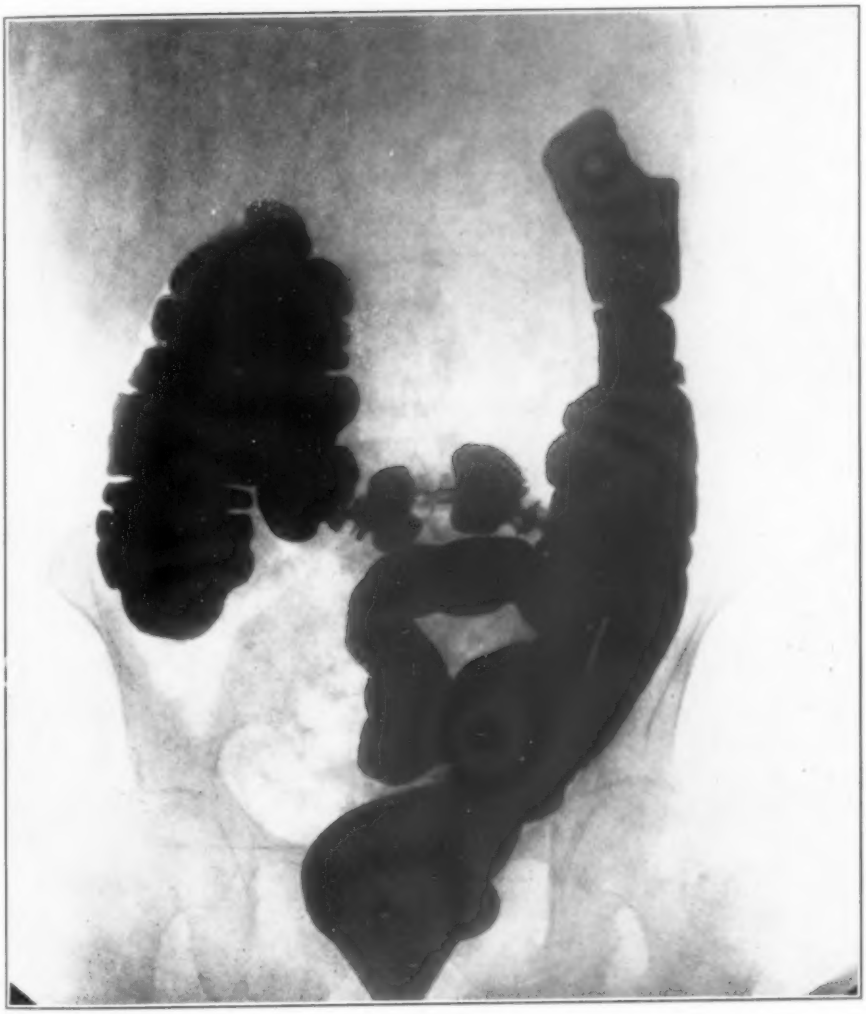

FIG. 10

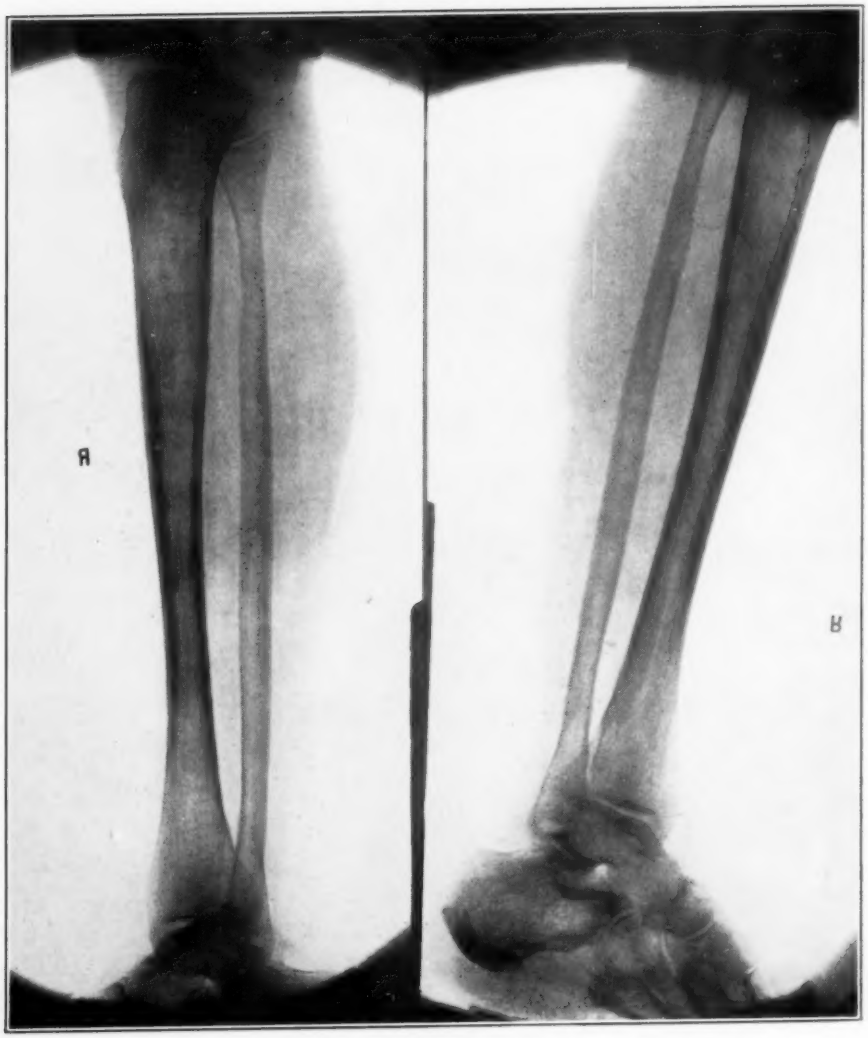

FIG. 11

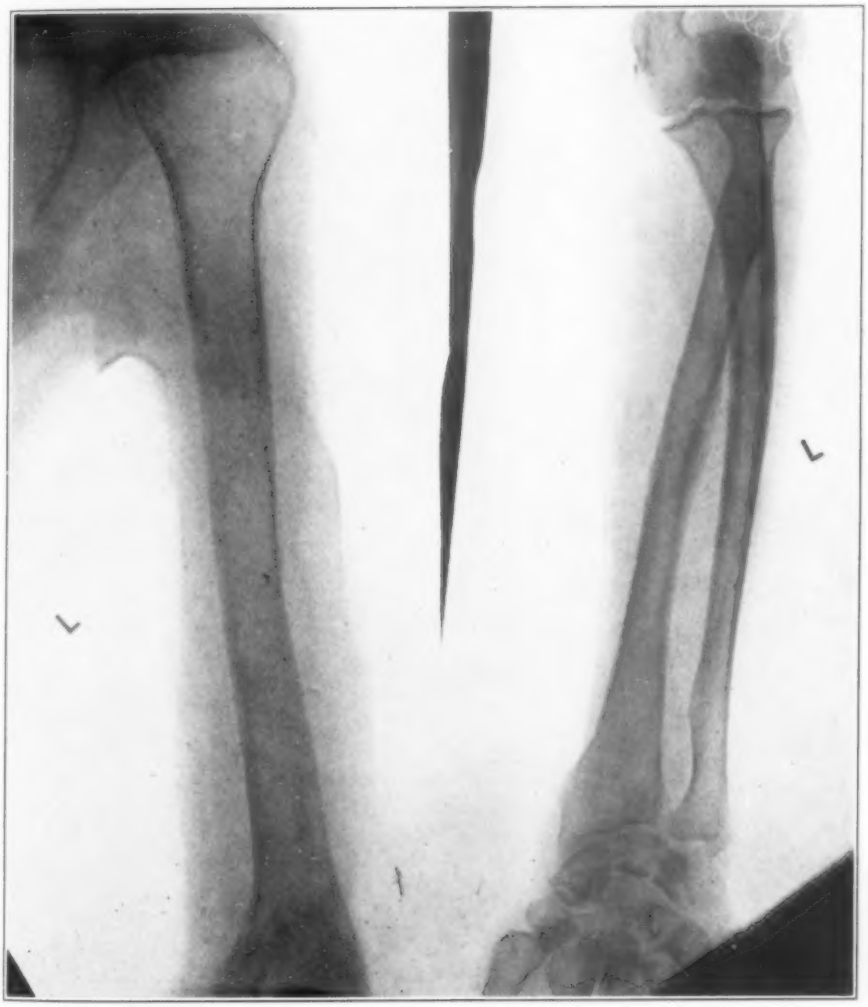

FIG. 12

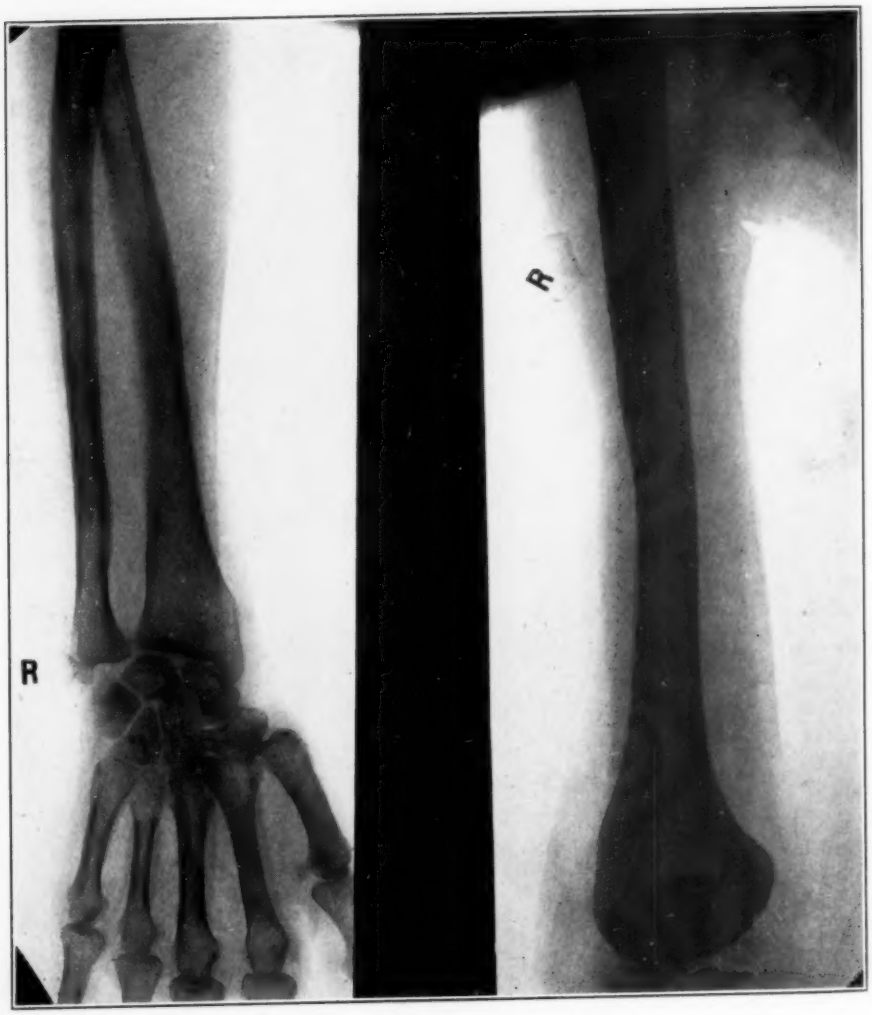

FIG. 13

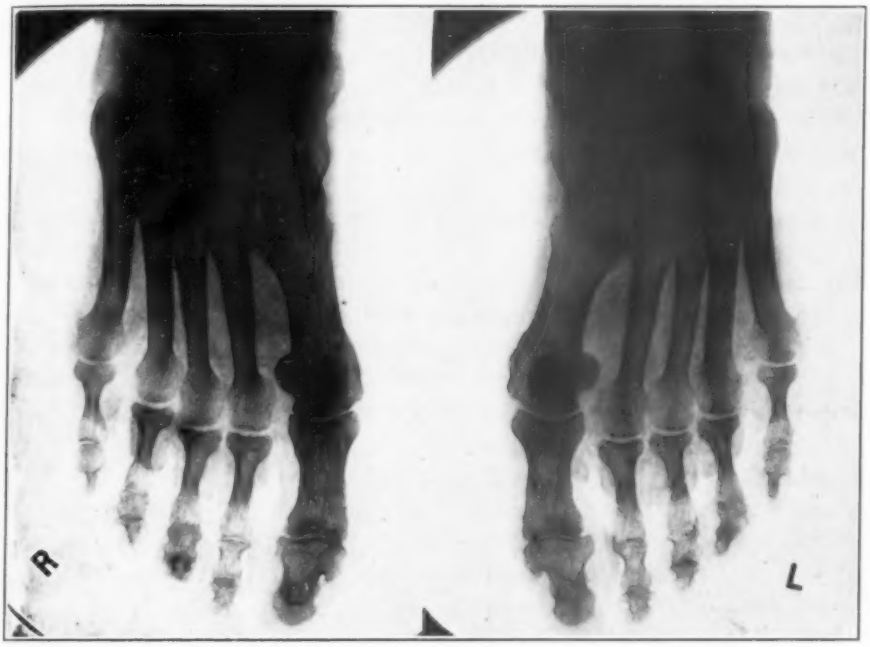

Fig. 14

differ in their clinical manifestations from the secondary multiple tumor formations in the bone marrow, in others, their clinical picture is identical.

The myelomas, depending upon their localization and distribution in the skeletal system, upon the intensity and direction of their growth, their anatomic relation to the compact bone substance, present a diversity of symptoms.

In some cases the symptom complex is very characteristic (Kahler): very severe pains, neuralgic like, over the thorax, mostly in the ribs, appearing in periodic intervals of several days. Sometimes, a deviation of the spine, or a definite kyphosis, the patient appearing smaller, will make the differentation from osteomalacia difficult. The ribs fracture at the least physical effort.

Secondary to such fractures a pleural effusion may follow (an exudate through inflammation of the pleura) accompanied by fever.

The elimination of the Bence Jones protein, which appears in the urine of 80% of the myeloma cases, although sometimes toward the end of the patient's life, usually one of the first symptoms, is regarded as the cardinal symptom of the disease. There is a very pronounced cachexia. The blood findings, as described in the literature, show little pathology except anemia.

Kahler in 1889 first described the above symptoms of the disease and held the circumscribed homologous tumor formations of the bone marrow responsible for the clinical symptoms

of the disease. The histological examination of his case (Chiari), showed that the tumors were multiple endotheliomas of the bone marrow. Further research has shown that primary multiple myelomas of various histological structure present the same clinical picture.

The case of Kahler was of a physician, 46 years old, whose disease started in 1879 with pains in the right side of the chest, which increased during respiration. The pains disappeared gradually, (few days), and returned after months localized in one point of the right 3rd rib, disappearing again after four weeks,—till 1880, in April, when the pains appeared in different regions, (ribs, vertebrae, left shoulder, left upper arm), increasing during motion. The processi spinosi of the vertebral column were sensitive. In March, 1881, a swelling appeared in the left fifth rib, which subsided after several weeks. Such periodic swellings, in different ribs, occurred often in the next years. Several nerve plexi became sensitive. In the urine the Bence Jones protein was positive. In 1882, the fingers of the hands, the cristae ossis ilei and the back of the head, became very painful, the gradually increasing cachexia forcing the patient to stay in bed. Paresthesia of the lower extremities, cardialgia and vomiting, enteralgia and asthmatic attacks, paroxysms of cough and chills complicated the condition. In the sixth year of the disease, a kyphosis in the upper dorsal segment started, the thorax became short, the vertebral column bent over more and more, the chin showed a decubitus from pressing on the chest.

The third right rib fractured spontaneously. Finally came disturbances of the sensorium, hallucinations and loss of consciousness. The cachexia became very pronounced, though still only a slight anemia.

Patient died after 8 years of illness. The post mortem showed numerous bone tumors which were called multiple myeloma. (Chiari held them for multiple bone endotheliomata).

Etiology

Trauma has been advocated as etiology by Gluzinski and Reichenstein, Heldt, Simmonds, Schennan, Weiss, Winkler; pains before the trauma, in some cases, a long interval between trauma and symptoms (Hopkins and Savory, Marchand, Funkenstein); trauma and symptoms at the same time, in the case of Ewald's rib fractures in Versé's case, where trauma happened 5 months previously. No trauma mentioned in Wallgren's cases. Infections accepted as etiology by Bechtold, Klebs.

Infections with fever in the cases of Hammer, Charles and Sanguinetti, Ellinger, Seegelken, Vignard and Gallavardin, v. Rusticky, Wieland and Zahn. The type of fever intermittent, due to the bone marrow process (Winkler), to bacteria in the blood (Beck and McClearly), or in diseased parts of the bone marrow (Bender, Madsen). Lues in the case of Bertoye. Lues and myeloma (von der Heide, Madsen, Wright, Parkes Weber.

Tuberculosis of the lungs (Abrikossoff, Zahn, Madsen, MacCallum,

Scherman, Saltykow, Taylor and Miller).

Primary anemia was thought to be the cause of the bone marrow changes by Grawitz.

In the case reported the history mentions a form of anemia in the mother and trauma at the beginning of the disease (the rib fracture which followed the trauma; the bone marrow condition may already have existed).

The age between 50 and 55 is most frequent for myeloma cases, as seen in Wallgren's table, reporting on 98 cases of anatomically certain myeloma; the youngest case at 22 (Haberfeld and Lordy), the oldest described by Grosch in a 80 years old woman. The disease is more frequent in men.

Pathology

According to the histological structure we distinguish two groups of primary multiple tumors of the bone marrow:

(a) the true multiple myeloma, circumscribed, the cells of which appear normally in the bone marrow tissue (parenchyma cells, colorless blood cells or normoblasts).

(b) the second group of primary multiple bone marrow tumors which have their origin in the stroma of the bone marrow (connective tissue or blood vessels): sarcoma, endothelioma, enchondroma.

The skeletal system in primary multiple myeloma presents deformities and spontaneous fractures. The thin corticalis at different places may resemble parchment. The tumors are mostly round, circumscribed, well demarcated from the surrounding bone marrow, gray, red or yellowish in color, resembling in sections, the structure of lymphatic glands. The most frequent localisations are the ribs, the vertebrae, and the flat bones, which contain red marrow. The tumors grow often in the compact portion of the bones, replace it and push the periosteum out forming round deformities. In other instances the tumors do not grow in the compact bone substance and do not produce deformities; they can only be detected within the bone marrow by sawing the bones. In the former instance, the bones are very soft and easily breakable (the ribs especially), the tumor mass having the consistency of white brain matter or spleen pulp. Often in post mortem, on a superficial observation of the skeletal system, serious changes are found, although one cannot macroscopically distinguish between the true multiple myeloma and the histologically differently constructed primary multiple bone tumors.

The presence of multiple myeloma is detected through bone enlargements, especially of the ribs, also the skull, sternum and hip bones. In the vertebrae and large bones the tumors are not protruding; in the case of involvement of the vertebral column, only if the protrusion effects a compression of the spinal cord does it become clinically interesting.

The sternum may become quite thick through the presence of tumor mass. Kyphosis and kyphoscoliosis of the vertebral column are also a frequent occurrence.

The term "multiple myeloma" was given by v. Rustitzky in 1873. He studied histologically and described one case from von Recklinghausen's

Institute. The tumors in his case had the consistency of white brain matter and presented the appearance of hypertrophied lymphatic glands. Microscopically the tumors were formed of round cells with an opalescent protoplasma and one or two round nuclei, little different from the surrounding bone marrow cells. On account of the identity of the tumor cells with the bone marrow cell elements, Rustitzky named the tumors myeloma, and wanted to emphasize that they have nothing in common with the myelogenous bone sarcoma (Virchow), which show a great many giant cells. The fact that the multiple bone sarcoma grows in the surrounding tissue, while the myeloma is strictly limited to the bone system, is another differentially diagnostic important feature.

Zahn in 1885, finds the analogy between myeloma and leukemic or pseudoleukemic hyperplasia, naming the former myelogenous form of pseudoleukemia.

Sternberg while he admits analogous changes of the bone marrow through myeloma, as the ones in the lymphatic glands and the spleen through pseudoleukemia, places myelomas on account of their localization and appearance in circumscribed, tumor-like formations, among the tumors, and due to their anatomohistological peculiarities, distinguishes them from pseudoleukemia.

Naegeli agrees to the similarity of myeloma with aleukemic systemic affections.

Grawitz describes them under the chapter of aleukemic medular hyperplasia.

Lubarsh sees in myeloma a systemic disease, very close to the leukemic and pseudoleukemic affections.

Schridde in his chapter on "The Blood-forming organs," describes myeloma as true bone marrow tumors, tumor-like hyperplasias of myeloid tissue, not easy to distinguish from leukemic myeloses. (Myelosarcoma are those tumors, which while made of myeloid tissue, produce metastases in other organs).

Kaufmann calls multiple true myelomas primary tumors of the bone marrow, composed of bone marrow cells.

Ribbert says: "In its structure the myeloma is close to lymphocytoma."

Pappenheim calls multiple myeloma a medullary form of pseudoleukemia, a systemic disease of the hemapoietic apparatus, of aleukemic nature.

Histologically, according to the kind of cells composing the myeloma, there are six different types of myeloma:—1). Myeloma composed of lymphocytes. 2). of myelocytes, 3). of myeloblasts, 4). of plasma cells, 5). of erythroblasts, 6). a mixed myeloma, in which all bone marrow cells are represented.

There is a definite differentiation between the medullary pseudoleukemia, which does not affect the compact portion of the bones, and the true multiple primary myelomas, which destroy it through a progressive resorption. The cases in which this peculiarity is not mentioned may have died before the growth of the myelomatous tumors was strong enough.

From the pathological histological point of view we define primary

multiple myeloma as tumors localized in the bone marrow, mostly circumscribed leukocytomas, having a tendency toward malignant growth but seldom leading to infiltration of the surrounding tissue or producing metatasis. Under certain circumstances they may not appear as isolated systemic diseases of the bone marrow, but rather, of the whole hemapoietic apparatus.

This purely histological definition should not lead to conclusions of any etiologic relation between multiple myeloma and the leukemic or aleukemic conditions.

Clinical Symptoms

The symptomatology of the primary multiple tumor formations in the bone system is practically the same, independent of the histological structure. The beginning of the disease is hardly noticeable. The patient very seldom knows the exact time when the first symptoms appeared.

In *Zahn's* case, intense pains in the region of the lower ribs and lumbar region followed exposure and strenuous work.

In *Hammer's* case, headaches were the first symptom, possibly due to the primary localization of the tumors in the bones of the head. In other cases, the pains started in the bones of the extremities or in the spinal column. Such conditions are apt to be regarded as rheumatism.

Often a trauma is given as history, and the disease followed, supposedly, several weeks afterwards; (cases of *Winkler*, *Ewald*, *Abderhalden* and *Rostoski* (after lifting a heavy load), *Gluzinski* and *Reichenstein*, *Hoffmann*, *Vance*). The trauma cannot be accepted as etiology, but helps to disclose the existence of the disease and the course may be hastened. The periodicity with which the pains appear and the pain-free intervals are characteristic. The localization is for the most part, in the thorax, vertebrae, hip bones, long bones, and only seldom in the head.

Cachexia very soon becomes pronounced but there are no signs of anemia.

The most evident symptoms are the bone deformities, such as deviation and bending of the spine, thickening of the ribs with nerve compression, and spontaneous rib fractures. Thorax deformities which impair the circulatory and respiratory functions produce dyspnea and cardiac oppression and may lead to secondary inflammatory conditions of the lungs, and so, to exitus; also, tumors in the vertebral column, with compression of the spinal cord, tending thus to exitus. The patients reach the state when they cannot leave their beds, develop decubitus and die from some complication.

The duration of the disease is on the average, from six months to one and one-half years, although there are exceptions, as in *Marchand's* case, which lasted six weeks, or in *Sussmann's*, which lasted three weeks, or in *Kahler's*, when the patient lived eight years. Men are more frequently affected than women, and generally between the ages of forty and sixty years.

Bone Symptoms

The tumors may not be detected intra vitam if they are very small or very few in number and do not produce any symptoms. Only in post mortems are multiple myelomas found in cases where they were not suspected.

The pains start in one bone and are most intense if the process involves the thorax, especially the ribs, giving a feeling of great oppression. The pains appear periodically or intermittently, increased through exertion. A severe sensitiveness of the bones is noticeable during pain paroxysms and also later. The intensity of the pains can be so great that the patient must keep to one position.

The patient of *Abrikosoff* started, as in my case, with pains in the left lower ribs, especially during motion. The percussion in such cases is painful.

The prominent symptoms (*Sternberg*) are,—very painful thickening of some of the bones,—sternum, ribs, skull, hip bones. The bone changes are seldom so evident as to be seen from a distance, except as in *Rusticki's* case, in which a tumor the size of a bean appeared on the left temporal side. It grew to the size of an apple, displaced the eye, injured the sight, perforated the bone and adhered to the dura mater.

Angular bending of the ribs occurs when the corticalis gets thin through the growth of the myeloma. Also, bending of the vertebral column, reducing the height of the patient, as in *Kahler's* case, who shrank to midget size. *Sternberg's* case had thorax deformity, the sternum S-shaped, and the vertebral column in a half circle.

The nerve plexi can be damaged through pressure, with resulting paraesthesia and nerve paralysis. In myeloma of the skull a stuporous condition is a usual symptom. Compression myelitis (*Rusticki's* case) is followed by paraplegia, incontinentia alvi and urinae.

Spontaneous fractures of the ribs caused by moving in bed or by percussion or palpation, are a frequent occurrence, and they represent the early symptoms of the disease.

Kahler's patient suffered immensely from the slightest motion and even from breathing.

Symptoms of the Nervous System

The nervous disturbances accompanying multiple myeloma may be the result of direct pressure of the tumors on a nerve plexus, the central nervous system, or in other cases of a toxic nature.

Paraesthesia is always a common complaint. Severe pains are localized in the bones seldom corresponding to one nerve. Skin hyperalgesia is a common symptom. Most important are the distrubances caused through compression of the spinal cord, followed by paraplegia, incontinentia alvi et urinae. Anomalies of reflexes are mentioned, without a definite pathology.

Stokvis mentioned in his case, paraplegia, speech and swallowing disturbances, salivation, trigeminus and facialis paralysis.

Wieland's case had hearing disturbances (labyrinth diseases).

Rustitzky's case started with a tu-

mor in the right temple, which gradually displaced the eye.

Quackenboss and Verhoff describe the protusion of the eye bulb through tumor pressure.

Heart and Lungs

The deformity of the thorax will bring about pressure symptoms of the heart and lungs.

Terminal pneumonias are quite frequent and also hydrothorax.

The digestive organs present also anomalies as anacidity, lack of appetite and intestinal paralysis (through direct cord lesions).

Cachexia is one of the most important symptoms, sometimes pronounced before definite bone symptoms are detected. A very severe general weakness, which begins early and progresses rapidly is another specific occurrence. The extremities are mostly affected, which forces the patients to leave the bed as little as possible.

The temperature is mostly normal, although there are instances, where a recurrent fever appears, sometimes chills and sweats, (Hirshfeld).

Blood Findings

The bone marrow in myeloma is replaced to a great extent by tumor masses; some parts, through pressure, being transformed into red marrow, we would expect serious changes in the composition of the blood.

A slight anemia is mentioned in most of the cases. (Anemia reported by: Austin, Beck and McClearly, Conti, Ellinger, Gluzinski, Haberfeld, von der Heyden, Jacobson, Kahn, Kimmerle, King, McCallum, Madsen, Mieremet, Schutz, Sexsmith & Klein, Stumm, Weber, Weinberg and Schwartz, Wallgren. (5 cases among 14).

Normal findings reported by: Bombard, Christian, Thomas, Jellineck, Kahn, McConnell, Martini, Scarlini, Vance, Wright, Wallgren. (5 cases).

The hemoglobin is found reported as low as 30% by Hertz and Jochmann-Schumm, 23% by Parkes Weber. Normoblasts and megaloblasts are mentioned by Gluzinski and Reichenstein. Lymphocytosis up to 60% and normoblasts in Voit-Salvendi and Hirschfeld cases.

Myelocytes, as pathological cells, are cited by Saltikow, Sternberg (21.8%), Parkes Weber, Wallgren. Eosinophilia cited in 6 cases by Wallgren.

Conti in his case mentions: Hem. 48%, Erythr. 1900000, L. 3400, (P. 42%, E. 4%, Ba. 2%, L. 14%, 1.10%, Mo. 22%, Myel. 6%.)

Arneth in his case found: Hem. 42%, E. 2400000, L. 10000. The percentage of the neutrophile polynuclears, was normal.

Kahn reports a pronounced anemia in two cases: 1). Hem. 34%, E. 3200000, L. 10200; (P. 63%, L. and 1.35%, Mo. 2%).

2). Hem. 30%, E. 2000000, L. 4800; (P. 49%, L. 42%, Mo. 9%); later: Hem. 18%, E. 1584000, L. 4200, (P. 60%, L. 36%, Mo. 3%, Ba. 1%).

Roman in his two cases observed in children, finds: Hem. 28%, E. 1900000, L. 9400, (P. 26, 8% E. 1.6%, L. 63, 8%, Mo. 5.8%, Meyl. 2%), and Hem. 40%, E. 1,500,000,

L. 9600 (P. 22%, L. 65%, Mo. 8%, Myel. 5%).

Sexsmith, found: Hem. 85%, E. 3140000, L. 8000; (P. 56%, L. 22%, Frans. 18%, E. 4%).

Martiri, found: Hem. 70%, E. 4877000, L. 6000; P. 61%, E. 1%, Mo. 10%, L. and 1.28%).

Kimmerle in his case: Hem. 70%, E. 3760000, L. 5700 (P. 60%, L. 30%, Mo. 6%, E. 1%, Trans. 3%).

McCallum reports as findings: Hem. 52%, E. 3548000, L. 4500.

McConnell: Hem. 80%, E. 4720000, L. 7200 (P. 58%, L. 7%, L. 30%, Trans. 5%).

The Urine

There is not another disease of the hemapoietic apparatus, in which the urine reports are of such importance. In some cases there is albumin and cylindruria, in a large percentage the appearance of the Bence Jones protein is of chief value. Up to 1910 (cases collected by Hirschfeld) 36 cases mention the presence of Bence Jones protein in the urine, while in 42 cases it was not detectable (in some, they may have neglected to look for it, in others the diagnosis of myeloma has been made only after post mortem).

Decastello found the protein in 2 cases of lymphatic leukemia, Askanazy also in a case of leucemia. Campbell Horsfall reports the presence of the protein in a case of gunshot under the knee; Zuelzer in dogs poisoned with pyridin.

The substance will be found in diseases involving the bone marrow, seldom in leukemias, most frequently in multiple myeloma. The cases of Fitz (myxedema and albumosuria) and of Coriat (Bence Jones protein in the pleural exudate of a case of Korsakoff's psychosis and myeloma), are doubtful in the opinion of Hirschfeld.

Bence Jones was the first in 1848, in a case of myeloma of Dalrymple and MacIntyre, to detect a protein which appeared in the urine, when heated to a temperature of 50 to 60 C, and which became soluble at a higher temperature (the case was diagnosed as osteomalacia fragilis rubra).

Stokvis in 1869, mentions the presence of the protein in a case of osteomalacia, Rustitzky in 1873, Kahler in 1889, Kaschker in 1894, report it in cases of senile osteomalacia.

Seegelken in 1896, in a case of chondro-sarcoma with albuminuria, Senator, Rosin, Süssmann, in 1897, in clinically evident cases of multiple myeloma.

Magnus Levy, in 1900, studied thoroughly the substance and found it to be a protein, not an albumose. Since then, we speak of a Bence-Jones proteinuria instead of albumosuria.

The protein is found in 80% of the primary multiple myeloma, hardly ever in metastatic bone tumors (Naunyn, Marcovici). The absence of the protein in cases of primary multiple myeloma, is mentioned by Scheele and Herxheimer, Collins, Wallgren (7 cases), while the presence is cited by Bradshaw (one year before the appearance of the tumors (an amount of 13.9 gr. per day), Oftedal, Cathcart (15 to 20 gr. per day), Groves (63 gr. per day), Auerbach, Sexsmith, Henderson (15 to 20 gr.),

Askanazy, Donetti, McCallum, McConnell, Buchstab and Schaposchnikow, Horsfall, Jochmann, Kimmerle (3 to 5%), Kahn in 2 cases, Wallgren (42 of the 118 cases in the literature, up to 1920).

The eliminated quantity reaches in some cases 70 gr. per day, the amount decreases or can disappear entirely toward the end of the patient's life. The substance may derive from the tumors or through their damaging influence on the remaining marrow. The detection of the protein in the tumors or in the blood serum has been negative in the literature as reported by Hirschfeld. Since then, the pressure in the blood is mentioned by Jacobson, d'Alloco, Martiri; in the spleen extract by Reach; in chloroma by Weinberger; in tuberculous osteoarthritis by Vidal; in myxedema by Jacksch, Fitz; in leukemia and in metastatic carcinoma by Boggs and Guthrie; in carcinoma ventriculi by Oerum; in ascite by Ellinger; in pneumonia sputum by Bradshaw; in bone marrow leukemia previously by Askanazy; in the pleural fluid by Goriat.

Decastello found serious changes in the kidneys accompanying the albuminuria (it is doubtful whether the kidney lesions are the primary moment allowing the passage of the protein, or the continuous passage of the protein damages the kidneys).

Massini finds that the amount of the excreted protein is equal to the amount of food protein taken.

(The reaction for the Bence Jones protein is very simple: the urine is tested for its acidity, acetic acid is added if found neutral, then heated between 40° and 60° degrees C.

A precipitate forms, which becomes soluble on further heating and reappears when getting cold. The substance gives all the color reactions for proteins).

Up to 1914, 61 cases were reported by Kahn of true primary multiple myeloma; 70 cases with post mortem reports are accounted for by Kimmerle, Schumm and Fraenkel.

Martiri's 206 cases may include some doubtful cases, since the very valuable contribution to the myeloma literature of Wallgren from 1920, reports only on 118 well studied cases, followed by post mortem examinations.

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Endocarditis Following Septic Abortion With Special Reference to Sub-Acute Bacterial Endocarditis*

By Carl H. Fortune, A.B., M.D., *Ann Arbor, Michigan*

THAT endocarditis, particularly sub-acute bacterial endocarditis, may be a sequel of infections during or following pregnancy, has received comparatively little attention, although many have considered the hazards incident to a pregnancy complicating a previously existing endocarditis. Acute malignant bacterial endocarditis, occurring more or less incidentally as a part of puerperal sepsis, has been recognized, and instances of this sort are common in any large series of cases of puerperal infection. By presenting three new cases from the Department of Pathology of the University of Michigan, this paper will endeavor to show that not only is acute malignant endocarditis a dreaded complication of puerperal infection, but that months afterward a typical sub-acute bacterial endocarditis may furnish a fatal sequel to an infected abortion which has passed the stage of acute manifestation.

In considering acute malignant endocarditis the differentiations made by Libman (1) will be accepted. He divides bacterial endocarditis into acute, sub-acute and chronic, considering the average course of sub-acute bacterial endocarditis as four to eighteen months, the acute cases being more fulminating. The infecting organism in acute endocarditis is usually streptococcus hemolyticus, although more rarely other organisms, such as staphylococcus, influenza bacillus, pneumococcus, etc., may be causative. The clinical course is that of a profound septicemia, with embolic phenomena as a prominent feature. Petechiae, sharp attacks of upper left quadrant pain, hematuria, etc., are seen. The physical findings on examinations vary somewhat according to the damaged valve. As pointed out by Libman (2), Herrick (3) and others, the process is particularly apt to attack a previously damaged valve. The following case is illustrative of this group.

Case I. Mrs. E. I., age 25, entered the University Hospital on the Gynecology Service, December 23, 1924, complaining of fever and bleeding from the vagina. Four weeks previous to her admission she stated that she had inserted a catheter into the uterus in an effort to produce abortion. Following this she passed two large blood clots, but experienced no profuse bleeding. After this she felt well and was able to perform her housework for a period of two weeks. At

*From the Department of Pathology, University of Michigan, Ann Arbor.

this time she again passed blood clots and bled profusely from the vagina for four days. Then she had a chill with fever of about 104 degrees and nausea but no vomiting. In spite of the severity of her symptoms she did not go to bed, but continued with her household duties. Bleeding continued until her admission to the hospital.

At the age of 10 she had an illness which she characterized as "rheumatism," but she stated that her joints were never swollen or red. She had no pharyngitis, tonsillitis or quinzy. Her catamenial history was negative and her last menstrual period was two months previous to her admission to the hospital. She had been married five years. Her husband was living and well. One child was living and well. There had been two previous abortions, one following a fall and the other induced by a catheter.

Physical examination showed the heart to be of normal size. Heart sounds were regular and of good quality. The first heart sound was replaced by a rough, low pitched, systolic murmur, heard best at the apex. The murmur seemed to extend back into presystole.

The abdomen was slightly tense in the lower quadrants. There were no masses, areas of tenderness nor muscle spasm. The spleen was questionably palpable.

Vaginal examination showed a foul, brownish discharge. The cervix was large and soft, showing a bilateral laceration. The uterus and adnexa were not palpated.

No petechiae were noted. There was no clubbing of the nails. No edema was present.

At this time the urine showed albumin four plus, many granular and hyaline casts, and strong tests for acetone and diacetic acid. The blood showed a secondary anemia, and a white blood count of 13,900 with 68% polymorphonuclear leukocytes. Blood culture was positive for streptococcus hemolyticus.

The patient was transferred to the Medical Service. During her stay in the hospital she had a septic fever, with chills followed by rise in temperature to between 103° and 105° with correspondingly rapid pulse and respirations. Repeated blood cultures were positive for streptococcus hemolyticus. Four days following admission she developed a right panophthalmitis and a bilateral acute arthritis of the wrists. She gradually became weaker, sank into a stupor and died on December 29, six days after admission.

Condensed Autopsy Protocol

Autopsy 97-AC. Prosectors: Drs. Simpson and Breakey. On external examination the body was seen to be that of a somewhat poorly nourished, but not emaciated woman of average build. Over the face were scattered pustules. The right eye showed purulent exudate covering the conjunctiva, with a clouding of the cornea so that the pupil could not be seen. The left eye was negative. Over the sacrum there was an area of decubitus measuring 5 x 4½ cm., appearing relatively fresh and covered by a dry reddish-brown crust. Herpes labialis was noted. There were no petechiae.

Examination of the brain showed no meningitis, but there was edema and congestion of the leptomeninges. The brain substance showed increased bleeding points and involving the left thalamus and part of the lenticulate and striate nuclei was an area of softening measuring 2 x 2 cm.

On making the main incision 75 to 100 cc. of thick fibrinopurulent exudate was found free in the peritoneal cavity. The pleural cavities contained no free fluid, but the pericardial sac contained about 40 cc. of thick purulent material. The heart was about the size of the cadaver's right fist. There was purulent exudate with some fibrin over the external surface. In the myocardium there could be seen pale localized areas appearing grossly as anemic infarcts, varying from 0.5 to 1 cm. in diameter. On opening the heart vegetations which had the appearance of being recent were seen on all the cusps of the aortic valve. Both flaps of the mitral showed vegetations, which appeared somewhat older, along their free edges and around the attachment of the chordae tendineae. The valve flaps were definitely thicker than normal, apparently due to an older healed inflammatory process.

The lungs were similar to each other and both showed an acute congestion. No infarcts were found.

On examination of the abdominal organs, the spleen was found to be about twice normal size. The capsule was smooth and had a reddish-blue color. Three anemic infarcts were present, one of which appeared to be infected. The splenic pulp was congested, and the Malpighian corpuscles were not readily seen. The gastrointestinal tract showed a fibrino-purulent exudate over the serosa. In the upper portion of the caecum there was a patch measuring 6 to 8 cm. in length where there was a diphtheritic membrane replacing the mucosa in an irregular pattern. The lymphoid tissue was hyperplastic throughout. A fibrino-purulent peritonitis was also present over the liver, which showed in addition considerable fatty change. The left kidney showed recent anemic infarcts. The parenchyma showed cloudy swelling.

The external genitalia were negative except for a thin leukorrheal discharge. The uterus was enlarged and soft. The tip of the finger could be inserted into the external os. There was a slight bilateral laceration of the cervix and slight eversion. The endometrium was bluish-red in color and in the fundus midway between the orifices of the Fallopian tubes was a mass measuring 3 x 1 x ½ cm., which had the appearance of retained, necrotic placenta. The uterine cavity was covered by a blood-stained fibrinous exudate. One tube was tightly adherent to the posterior surface of the uterus. One ovary showed a large corpus hemorrhagicum.

Microscopic Examination. Dr. Warthin

Heart: Active streptococcus endocarditis on an older thickened endocardium. Streptococcus abscesses in myocardium. Older areas of fibrosis in myocardium. Marked fatty degenerative infiltration, both subepicardial and subendocardial. Localized acute fibrino-purulent epicarditis over abscess in the myocardium. Abscess in subepicardial fat. Marked tiger heart.

Uterus: Infected placental site. Necrotic decidua. Diffuse diphtheritic endometritis. Streptococcus infection following abortion.

Fallopian Tubes: One shows an acute perisalpingitis with plications infiltrated with polymorphonuclear leukocytes. Other tube practically normal.

Vagina: Acute vaginitis.

Pathological Diagnosis: Streptococcus septicopyaemia (following self induced infected abortion). Diphtheritic endometritis. Acute purulent salpingitis. Generalized fibrino-purulent peritonitis. Acute mitral and aortic thrombo-endocarditis. Multiple streptococcus emboli with recent infected infarcts in spleen, kidneys, myocardium and brain. Localized acute purulent meningitis and pericarditis. Right-sided purulent panophthalmitis. Acute diphtheritic colitis. Pyoderma of face. Herpes simplex labialis. Acute passive congestion and parenchymatous degeneration of all organs. Tiger heart. Old appendectomy scar. Decubitus.

Cases similar to this are numerous in the literature. Westphal (4) reported such a case in 1861, and in 1872 Virchow (5) reported a series of such cases, and pointed out the importance of endocarditis as a phase of puerperal sepsis. Recently, Mathias and Pietrusky (6) in analyzing 55 cases from the Pathological Institute at Breslau found 7 cases of fresh endocarditis. The illustrative case cited has all the clinical features of an acute endocarditis. The source of the infection is readily discernible, as is usual in acute endocarditis. The rapid course, blood cultures positive for streptococcus hemolyticus and embolic phenomena, are all typical. The necropsy findings were characteristic

throughout and established the connection between the infected abortion and the endocarditis.

Sub-acute bacterial endocarditis shows a definite clinical difference from the acute type. The onset is characteristically insidious as compared to the more sudden onset of acute endocarditis. A general malaise, weakness, and lack of tone are usually the first symptoms. At this time there is usually an irregular fever, and often chills, but the patient is often able to perform her duties. What might be characterized as the terminal stage of the disease may be ushered in by embolic phenomena, and these are nearly always present at some time before death. Particularly are petechial hemorrhages usually seen at some period during the patient's illness. Blood cultures are frequently positive, although cases are reported with a typical clinical course and characteristic necropsy findings where the blood culture has been consistently negative. The course of the disease has generally been considered to be progressively fatal although Libman (7) has reported clinically cured cases. The duration varies from six weeks up to two or three years in exceptional cases. Often there are periods of recession of the disease followed by relapses, although the condition may be steadily progressive. The following two cases are submitted as typical sub-acute bacterial endocarditis following infected abortion.

Case II. Mrs. M. C., age 19, entered the Internal Medicine Service of the University Hospital September 14, 1919, complaining of weakness and loss of weight. She was married and had one child 15 months old. As a child she had measles and chicken-pox with good recovery. At the age of 12 she had typhoid fever, and stated that she was very ill for several weeks. Since that time she had enjoyed good health until the onset of the illness which caused her to come to the hospital. Her health since marriage had been as good as previously.

In February, 1919, she was pregnant about two months. Following the advice of a neighbor, she induced an abortion by passing a catheter, which she had made no attempt to sterilize, into the uterus. The abortion followed three days after the instrumentation. At this time she felt "sick at her stomach," and for a period of two weeks she had fever and several chills. She had never felt well since that time. There was a thick yellowish discharge from the vagina, but she experienced no pain except for painful urination for a short time. She had noticed loss of weight, although she did not know how much, and said her heart pounded and was irregular. These symptoms increased and she became weaker until finally she consulted a physician, about August 1, who put her on a liquid diet. She followed this treatment at home for three weeks and then entered a hospital in another city where she remained twenty days, steadily growing worse. At the end of that time she came to this hospital.

Physical examination showed a small woman of anemic appearance, with a faint flush over the cheeks and a slight cyanosis of the lips. The nodes of the posterior cervical chain were slightly enlarged and tender. There was a bounding pulsation of the great vessels of the neck with definite venous pulse.

Examination of the heart showed the apex beat to be visible in the precordium. The cardiac rhythm was regular but rapid. The first sound at the apex was ringing and accompanied by a soft systolic murmur. Immediately following the first sound and replacing the second sound was a loud, blowing diastolic murmur, lasting throughout diastole, and well transmitted to the axilla. Over the aortic area there was a loud murmur lasting throughout systole and immedi-

ately followed by an equally loud murmur lasting throughout diastole.

Examination of the lungs show impairment of percussion resonance at both bases. Breath sounds in these regions were faint and distant, and deep inspiration brought out a coarse friction sound. Examination of the abdomen was negative. Neither liver nor spleen could be felt. The fingers showed clubbing and curving of the nails. There was no edema of the extremities. No petechiae were seen.

During her stay in the hospital, she had a rise in temperature every afternoon. Six days after admission the patient complained of pain over the heart and experienced difficulty in breathing. The next day she was drowsy and during the afternoon she had the usual rise in temperature, became restless, and the pulse became more rapid. The next morning she was dyspneic, cyanotic, and showed a very slow labored pulse. Respirations gradually became slower and more labored, and she died quietly at 6:55 A.M., September 22, eight days after entering the hospital.

Condensed Autopsy Protocol

Autopsy 26-X. Prosector: Dr. Weller. The body was that of a young adult female of slight build, showing fair nutrition, but marked pallor. The main incision showed no free fluid in either abdomen or chest.

The heart was markedly enlarged and showed no evidence of pericarditis. On opening the heart, the mitral cusps were seen to be beaded with organized and ulcerated vegetations. In the right cusp there was an aneurysm measuring 5 mm. in diameter. All the cusps of the aortic valve showed an extreme degree of ulceration, one being eroded until only about 3 mm. remained. From the edges of this extended stringy masses of fibrin. These vegetations extended up into the first portion of the aorta.

The lungs showed congestion but there was no consolidation. The abdominal examination showed a spleen four times normal size. The splenic pulp was hyperplastic, and there was marked congestion. There was one small anemic infarct measuring 3 x 5 mm. The kidneys were slightly larger than normal. There was well marked cloudy swelling, and in the left kidney a small area of partly healed anemic infarction. Otherwise the abdominal examination revealed nothing of interest.

Coming from the vulva was an abundant purulent discharge, smears of which showed streptococci and bacilli. There was a small amount of exudate over the endometrium, but no severe process. The uterus was of about normal size. Ovaries were normal in size and showed no large corpora lutea.

Microscopic Examination. Dr. Warthin

Heart: Fatty infiltration with serous atrophy. Marked atrophy and fatty degenerative infiltration of heart muscle. Organizing vegetations. Sub-acute endocarditis.

Spleen: Marked chronic passive congestion. Lymphoid atrophy. Exhaustion of germ centers.

Kidneys: Cloudy swelling. Atrophy. Congestion. Serous atrophy of the subpelvic fat. Areas of chronic inflammation. Fresh anemic infarcts.

Uterus: Endometrium atrophic. Small leiomyofibroma.

Ovaries: Chronic ovaritis and periovaritis. Imperfectly resolved corpora fibrosa with calcification.

Tubes: Negative.

Pathological Diagnosis: Sub-acute thrombo-endocarditis of mitral valve with valvular aneurysm. Ulcerative endocarditis of aortic valve. Aortic stenosis and insufficiency. Cardiac dilatation and hypertrophy. Anemic infarction of spleen and kidney. Severe secondary anemia. Serous atrophy of fat tissue. Marked fatty heart. Tiger heart. Passive congestion and parenchymatous degeneration of all organs. Streptococcus septicaemia (post-abortion).

Case III. Mrs. E. O., American housewife, of 18 years, entered the Neurological Service of the University Hospital on the

21st of November, 1927, complaining of paralysis of the left side of the body, pain in the right calf, and general malaise and weakness.

The patient was married at 13. She had one child 3 years old, living and well. She had had about seven self-induced abortions, the last one in July, 1927, when she was about 4 months pregnant. She was taken to a hospital at that time. Ever since that time she felt below par, although she had no definite symptoms with the exception of a foul discharge from the vagina. About three weeks before entrance, after pumping a pail of water and walking back to the kitchen, it was noticed that the right side of her face was pulled out of shape. The left arm and leg became paralyzed and she was unable to walk. She was not unconscious. She was again in the hospital for a short time and partially regained the use of her left leg. The left arm and the left side of her face remained paralyzed.

Physical examination disclosed a well-nourished and well-developed young woman of poor mentality who coöperated fairly well. She did not, however, know her age exactly. Examination revealed a hemiplegia, most marked in the face and arm, the patient having partial use of the left leg sufficient to enable her to stand and walk lamely. The heart was slightly enlarged to percussion. There was a systolic murmur heard over the aortic area which was blowing in character and a very faint diastolic murmur. The pulse was of the Corrigan type; the blood pressure 135/20. The liver and spleen could not be palpated because of voluntary abdominal rigidity. Pelvic examination revealed retroversion of the uterus, which was enlarged and boggy. There was a brownish discharge which was foul.

Blood Wassermann was negative. On the 25th a blood culture showed Gram positive cocci, probably streptococcus viridans. The urine showed a moderate amount of albumin, hyaline and granular casts, occasional red blood cells and many white blood cells. The blood showed hemoglobin, 50%; red blood cells, 2,500,000; white blood cells, 7,600; differential: — polymorphonuclears, 73%; lymphocytes, 13%; endotheliocytes, 8%. The electrocardiogram showed marked sinus tachycardia, but was otherwise normal. The X-ray on November 23rd showed cardiac enlargement, flattening of the left auricular curve, and clear lung fields.

The temperature fluctuated from 100° to 102°. During the latter part of her stay in the hospital her pulse averaged about 130; respirations, 40 to 68. On November 29th, the lungs, which had previously been clear, revealed râles and bronchial breathing in the lower right chest and a somewhat more marked involvement of the left. The liver at this time was palpated one hand's breadth below the costal margin. Her symptoms became progressively worse and she died December 1st.

Condensed Autopsy Protocol

Autopsy 103-AF. Prosectors: Drs. Weller and Fortune. The body was that of a well developed young adult female, showing no evidence of loss of weight. The skin had a noticeably gray tinge. There was lack of tone in the muscles of the left side of the body. Rigor mortis had not set in. Edema was present in both ankles, but more marked on the left.

In the right temporal lobe there was an area of softening measuring 5 x 5 x 5 cm., extending back into the basal ganglia, giving an area of softening in the floor of the right lateral ventricle. The right cerebral peduncle also showed an area of softening.

The heart was much larger than the cadaver's right fist, measuring 12 x 10 x 5 cm., and weighing 410 gms. There was a small soldier's spot on the anterior surface of the right ventricle and on the posterior aspect of the left ventricle there was a sharply localized area of adhesion between the parietal and visceral pericardium. On opening the heart there were many ulcerating vegetations seen extending along the edge of the aortic flap of the mitral valve for a distance of one centimeter. One centimeter above this line of vegetations there was a nipple-like projection 5 mm. in its diameter extending into the left auricle. On investigation from below this was seen to be an aneurysm of the flap. Just below

the cusps of the aortic valve were numerous vegetations, completely surrounding the orifice and extending up onto the cusps. This process was much more marked than on the mitral valve. In the right ventricle on the septum, just opposite the mass of vegetations described below the aortic valve, there was a projecting mass of vegetations, which proved to be a mycotic aneurysm extending through the septum from the left heart. This aneurysm involved the flap of the tricuspid valve adjacent.

The lungs showed a brownish color, but not the firmness of induration. There was a marked congestion. Both lungs contained hemorrhagic infarcts, the largest of which was in the lower lobe of the right lung, and had a base 8 cm. in diameter with a fibrinous pleuritis over the surface. The pulmonary vessels contained thrombi, some of them old and yellowish-white in color. On section of the spleen numerous small subcapsular infarcts were seen. The kidneys showed both old healed infarcts and more recent infarcts, some of them very fresh.

The cervix uteri showed a large polypoid mass projecting through the external os. The upper attachment of this mass was in the uterine cavity at the right upper pole. This was covered by purulent exudate and had the appearance of an infected fleshy mole. The endometrium was hyperplastic and congested. The left ovary showed a large corpus luteum. The tubes appeared negative except for congestion.

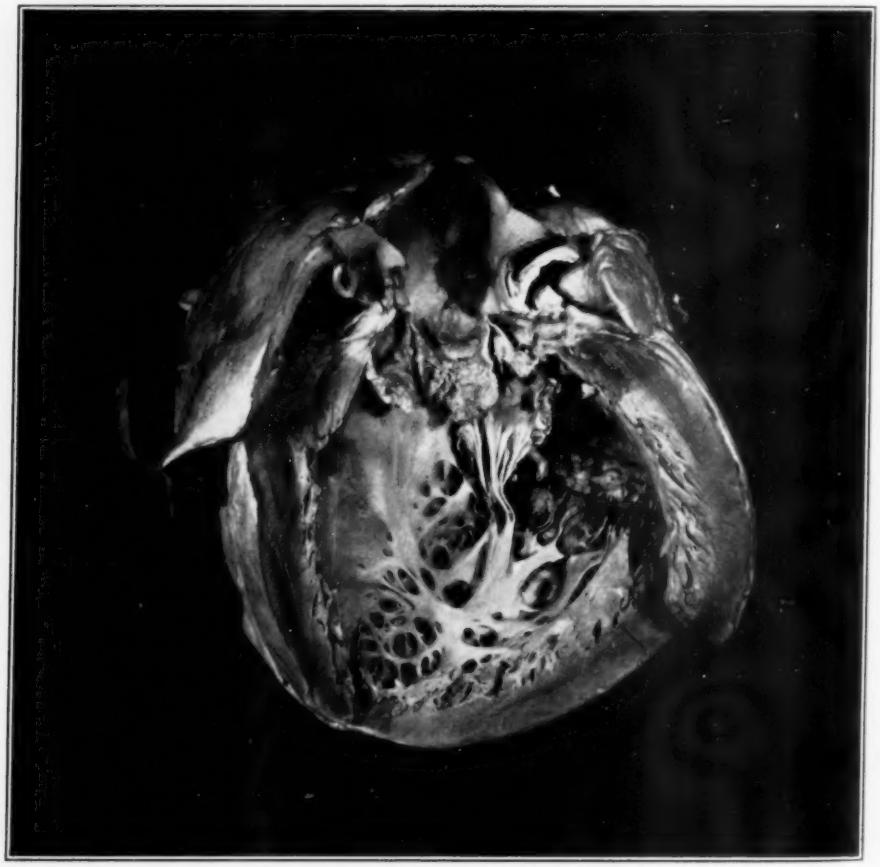

FIG. 1. Heart from Case III, showing vegetations on the aortic valve.

Microscopic Examination. Dr. Warthin

Brain and Meninges: Marked congestion and edema. Localized meningeal reaction over the areas of softening. Multiple large areas of anemic softening scattered throughout the brain, in both cerebrum and cerebellum. Most of these are very recent as there is very little proliferation about the borders. No sclerosis of meningeal or cerebral arteries.

Heart: Subepicardial fatty infiltration. Diffuse fatty degenerative infiltration, most marked under the endocardium. Extreme tiger heart. Muscle fibers are atrophic. Subacute bacterial endocarditis, still in active stage. Sclerosis of endocardium, with fresh vegetations on surface containing large bacterial colonies. At the base of these vegetations small tears extend through the thickened, inflamed endocardium—first stage of aneurysm formation. Coronaries show slight lipoidosis of intima. No areas of either active or healed myocarditis.

Lungs: Extreme congestion and edema. Multiple thrombosis of pulmonary veins. Multiple hemorrhagic infarctions. Extreme edema. Numerous pigmented "Herzfehler" cells but no induration of lungs. Areas of marked atelectasis with acute purulent bronchitis and beginning broncho-pneumonia. Fat stains show no fat emboli.

Spleen: Extreme congestion. Multiple infected anemic infarcts. Infected emboli. Marked necrosis of the splenic follicles.

Kidneys: Congestion. Atrophy. Slight cloudy swelling. Very few scarred glomeruli, except in areas of healed infarcts. Multiple anemic infarctions in all stages, some wholly recent; others healing. Fat stains show practically no lipoidosis.

Cervix of Uterus: Severe glandular erosion. Chronic catarrh.

Body of Uterus: Localized polypoid cystic glandular hyperplasia. Extreme congestion. Some blood pigment. Vessels show resolution—post pregnancy. Incomplete resolution. Cavity of uterus filled with a fleshy mole containing necrotic and still living chorionic villi, decidua and infected blood clots. Infected retained placenta following abortion. In the uterine and vaginal plexus there are infected thrombi.

Ovaries: Unresolved corpus luteum. A few cystic follicles.

Tubes: Subacute inflammation.

Pathological Diagnosis: Septicopyaemia (streptococcus). Retained infected abortion. Sub-acute septic vegetative endocarditis involving aortic and mitral flaps. Valvular aneurysm of mitral cusp. Mycotic aneurysm between root of aorta and right ventricle. Multiple embolic infarcts of brain, spleen, kidneys, lungs and abdominal wall. Early pyaemic abscess formation. Marked fatty degenerative infiltration of heart muscle. Extreme nutmeg liver. Marked passive congestion of all organs. Simple colloid goiter.

Discussion

In both of these cases it will be noted that from a clinical point of view, the onset was insidious and not accompanied by characteristic symptoms. This period preceding the onset of serious symptoms was long, in one case six months, in the other case more than four months. In Case III brain embolism initiated the final stage of the disease, in Case II there were simply increasing weakness and disability. Unfortunately no blood culture is recorded for Case II. In Case III streptococcus viridans was present intra vitam, and a blood culture was taken from the heart post mortem and showed also characteristic streptococcus viridans. Both cases showed during their stay in the hospital the usual findings of a septic endocarditis.

Pathologically all three cases are typical vegetative thrombo-endocarditis. It will be noted that there is no characteristic difference post mortem between acute malignant endocarditis and sub-acute bacterial endocarditis, except for the fact that in the case of sub-acute bacterial endocarditis the heart lesions are, as the name implies, in the sub-acute stage and some of the embolic lesions are generally in the healing stage. In Cases I and III the infective process was still active in the uterus, in Case II this had subsided to a considerable degree. However, the exudate from the uterus and vulva still showed streptococci, and with the clear clinical history connecting the endocarditis with the abortion, there seems no question but that it should be considered as a sequel of a postabortal sepsis. In the acute case it will be noted that there was a generalized peritonitis which might well be considered as a direct extension from the uterus. In the sub-acute cases, however, the secondary foci of infection were all such as might well be attributed to the heart lesion. In other words, the endocarditis was apparently the only process of infection resulting from the puerperal sepsis and the lesions throughout the body were secondary to the process in the heart. Without an association of the clinical and necropsy findings, the connection between the abortion and the endocarditis might well be missed in such cases.

Pathologically Cases II and III are interesting quite aside from the connection between the abortion and the endocarditis. Both cases showed aneurysms of the mitral valve. In Case III there was in addition to this a mycotic aneurysm at the base of the aortic valve extending through into the right ventricle, involving the tricuspid valve. Mycotic aneurysms are not unusual in bacterial endocarditis, but it is rare to have the tricuspid valve involved by vegetative endocarditis, and still more rare to have it involved by an aneurysm arising on the other side of the heart and passing through the septum. The presence of these vegetations in the right side of the heart explains the occurrence of the hemorrhagic infarctions in the lung found in this case.

These three cases call attention to the fact that endocarditis, whether acute or sub-acute, is pathologically the same condition, the variation in the clinical picture being largely dependent upon the virulence of the infecting organism. The fact that bacterial endocarditis is particularly prone to attack a previously damaged valve, has been emphasized by Libman (2), Herrick (3) and others. In one of the cases presented, there was a healed endocarditis of the valve, which preceded the more recent process. In another there was sclerosis of the endocardium, which may have indicated an older endocarditis. It has been generally accepted that in sub-acute bacterial endocarditis the source of infection is not apparent, and such "foci of infection" as tonsils, teeth, etc., have been given prominence as source of entry for the infecting organism. The question may well be raised whether in many of the cases the element of time has not obscured an evident source of infection. For example in a case of septic abortion,

following the infection in the uterus, there is entrance of organisms into the blood stream. If one of the valves of the heart has been damaged by a previous endocarditis, there is a locus of lowered resistance at which the organisms may settle out. If the infection is with streptococcus hemolyticus, the patient may have a typical acute endocarditis septicaemia; if it is streptococcus viridans she may six months later develop a sub-acute bacterial endocarditis, which neither pathologist nor clinician may associate with the abortion.

No attempt is made to assert on the basis of such a small number of cases, what is the frequency with which sub-acute bacterial endocarditis follows an infection of pregnancy. Neither is there any attempt to refute any established beliefs concerning the origin of the infection in other cases of bacterial endocarditis. However, with these cases in which the connection seems well established, and recognizing the pathological similarity of the sub-acute forms to the acute forms, it seems justifiable to call attention to the possibility that sub-acute, as well as acute bacterial endocarditis, may be a frequent complication of puerperal sepsis. If this be so, the careful internist in investigating a case of sub-acute bacterial endocarditis, occurring in a woman of child-bearing age, must consider the possibility of an infection of pregnancy as a possible source for the infecting organisms of the endocarditis. Furthermore, the obstetrician who has a case of puerperal infection, or infected abortion, under his care must bear in mind the possibility that even though the acute manifestations of the disease are successfully passed, there is still the possibility that an endocardial involvement may occur at a later period. The instances cited emphasize the danger of an untreated septic abortion, since all the cases of endocarditis following abortions which have come to our attention had received no medical treatment until the sepsis was well established. It seems quite possible that thorough and prompt removal of the infected focus in the uterus might prevent such cases of delayed endocarditis and even perhaps the cases of more acute endocarditis.

Summary

Three additional cases of bacterial endocarditis resulting from uterine infection following abortion are presented. Attention is called to the well-established fact that an acute endocarditis is a frequent and serious complication of puerperal sepsis. One of the cases presented is illustrative of this type of cardiac disease. Sub-acute bacterial endocarditis, while differing clinically in its course, is recognizable as being the same pathological process, differing only in stage, the clinical peculiarities being due probably to the type of infecting organism. The other cases illustrate the fact that sub-acute, as well as acute, bacterial endocarditis may be a complication of infection following abortion. In these instances the cardiac condition dominates the clinical picture, and the connection with the previous abortion is easily overlooked.

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Familial Glycosuria. Report of a Large Family.

By Harold M. Bowcock, M.D., *Atlanta, Georgia*

THE familial occurrence of glycosuria is attracting increasing interest and families displaying this symptom in several members deserve special study. Joslin (1) records a family in which twelve brothers and sisters, and two children are thought to have had diabetes. He reports a Jewish family, eight members of which had diabetes. Landis (2) reports a diabetic family in which the disease was present in the five blonde but not in the four brunette children of a diabetic mother. These are striking examples of families in which all of the individuals showing glycosuria are sufferers from diabetes.

Additional large families have been studied in which non-diabetic as well as diabetic glycosuria has been present in several members.* Holst (3) gives a good bibliography of the Scandinavian literature and reports eleven families in which two or more members displayed glycosuria; the largest number of glycosuric members in a family was eight. The largest number of diabetics in any of these families was four; the remaining members showed a benign glycosuria. In each of ten of these families the blood sugar reaction of one member was studied after the administration of glucose; two members of the eleventh family were studied in this manner. Hatlehol (4) reports twelve families, members of which showed benign glycosuria; diabetes was present in five of these families. Malmros (5) reports a family in which 12 members showed glycosuria in the absence of any symptoms of disease.

The following report is concerned with the study of a family in which eighteen members show the presence of a reducing substance in the urine in the absence of any symptom of diabetes. Figure I shows the family tree, designating the affected members. In five members the blood sugar response to glucose administration by mouth has been studied; the resulting curves display, in one case, the reaction characteristic of mild diabetes mellitus; in two cases the result is typical of renal glycosuria; in two cases, of cyclic renal glycosuria; and in thirteen members the type of blood sugar response has not been studied.

The urine specimens from those members of the family whose responses to glucose have not been studied were collected about two hours after the largest meal of the day because such postprandial specimens are the ones most likely to contain glucose.

*Hjärne (Acta Med. Scandinav. 67, p. 422, quoted by Malmros) studied 199 members of a family and found glycosuria in 41 members.

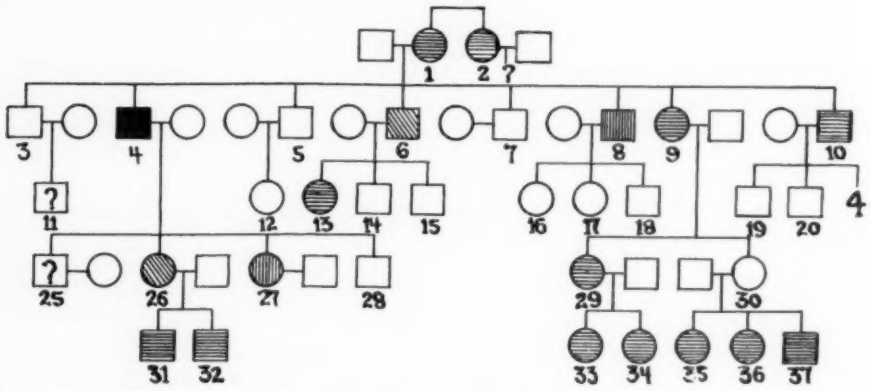

CHART I. Family tree. Legend: The square symbols represent males; the circular symbols represent females. The numbers under each symbol correspond to the member number in the text. Solid black represents diabetes; diagonal hatching represents renal glycosuria; vertical hatching represents cyclic renal glycosuria; horizontal hatching represents glycosuria of an undetermined type; the urine of members represented by plain symbols did not contain glucose. The urine of those designated by an interrogation mark has not been tested.

The three types of glycosuria mentioned above have the following characteristics:—The mild diabetic (6) displays a fasting blood sugar slightly above the normal, accompanied by the presence or absence of sugar in the simultaneous urine specimen. Following the administration of glucose by mouth, the blood sugar rises to an abnormally high level, usually reaching the peak of the rise only after an hour's time, accompanied by the appearance of sugar in the urine. The blood sugar level then decreases slowly and is still above normal at the end of three hours.

With renal glycosuria, the fasting blood sugar level is normal or low, and the simultaneously voided urine contains sugar. Following the administration of glucose by mouth, the blood sugar level does not as a rule rise even as high as in the normal individual; the peak of the rise is usually reached within forty minutes and within two hours the blood sugar has returned to a normal level. Varying quantities of sugar are excreted in the urine throughout the test.

With cyclic renal glycosuria (7, 8) the fasting blood sugar level is normal and the simultaneously voided urine is sugar-free. Following the administration of glucose by mouth, a curve similar to the normal blood sugar response is observed. Accompanying the normal rise in the blood sugar the simultaneous urine specimens begin to contain sugar at a blood sugar level, usually between 120 and 140 milligrams per 100 cc of blood, demonstrating a low renal threshold for glucose. In other words, glucose appears in the urine only after the ingestion of food or glucose, while in renal glycosuria the urine usually does not become sugar-free even during periods of fasting.

Report of Family

The urine specimens from thirteen glycosuric members of the family have been studied by the author, who is indebted to Dr. J. L. Porter for his assistance in discovering glycosuria in several of the members studied. Dr. N. Peterson and Dr. J. B. H. Day determined the presence of a reducing substance in the postprandial urine of other members of the family. It is unfortunate that some members could not be located, and that two declined to submit specimens for examinations.

Member 1. White female, aged 78, has been obese but is now thin. A recent specimen of urine contained a large amount of reducing substance.

Member 2. White female, aged 70, a sister of member 1, is said to be thin. A recent urine examination showed a trace of reducing substance.

Member 4. White male, aged 56, a son of member 1, was seen April 13, 1927. His past history was unimportant except for frequent attacks of epigastric pain as a young man; these attacks had occasionally required a hypodermic of morphine for relief. He had passed his urine one to three times during the night for fifteen years, but had had no other symptoms of diabetes. He had never weighed more than 145 pounds (65.9 Kg) until he stopped smoking during 1919; following this he had gained weight rapidly and had reached his greatest weight of 207 pounds (94.0 Kg) one month ago. He had exhibited a slight elevation of blood pressure. Sugar had been discovered in his urine during a life insurance examination in 1923. He had not followed a diet and occasional subsequent urine examinations had always shown sugar. His height was 5 feet 6 inches (167.6 cm.) and his naked weight was 196 pounds (89.1 Kg). Table 1 shows his blood and urine response to glucose, displaying the type of reaction observed in the mild diabetic.

Member 6. White male, aged 36, a son of member 1, was seen Jan. 1, 1927. His past history was unimportant. Starting three years ago he had had nycturia one to three times, some polyuria and marked urgency; during the past year he had not had to pass his urine during the night. He had had no other symptoms of diabetes. Sugar had been discovered in his urine during a life insurance examination in 1916, at which time he had weighed about 150 pounds (68.2 Kg). Later, the sugar had disappeared and he had been able to obtain insurance. His urine has continued to show sugar at times. His greatest weight had been 175 pounds (80.0 Kg), two years ago; his average weight was 160 pounds (72.7 Kg). His height was 5 feet 8¾ inches (174.6 cm) and his naked weight was 155 pounds (70.5 Kg). Table 1 shows his blood sugar curve and urine findings after glucose. The type of response is characteristic of renal glycosuria, although the history of becoming sugar-free at times, suggests cyclic renal glycosuria.

Member 8. White male, aged 43, a son of member 1, was examined Nov. 24, 1926. His past history was unimportant. He had been rejected for life insurance during 1916 because of sugar in his urine, at which time he had weighed about 170 pounds (77.3 Kg). He had restricted carbohydrates for six months following this experience and had then been accepted for insurance. There had been no subsequent urine examination. He had passed his urine once or twice during the night for about 10 years, but had had no other symptoms of diabetes. His average weight was 180 pounds (81.4 Kg) and his greatest weight had been 190 pounds (86.4 Kg) one year ago. His height was 5 feet 9½ inches (176.5 cm.), and his naked weight was 178 pounds (80.9 Kg). Table 1 shows the blood sugar and urine findings after glucose; the type of reaction is characteristic of the condition described as cyclic renal glycosuria.

Member 9. White female, a daughter of member 1, is said to be very obese. A recent urine examination showed the presence of a small amount of reducing substance.

TABLE 1—GLUCOSE TOLERANCE TEST

Member Number	Member 4			Member 6			Member 8	
	Blood Sugar in mg. per 100 c.c.	Urine Volume	Urine Sugar	Blood Sugar in mg. per 100 c.c.	Urine Volume	Urine Sugar	Blood Sugar in mg. per 100 c.c.	Urine Sugar in grams
Fasting	122	50 c.c.	0	87	20 c.c.	Trace	105	0
100 grams glucose as lemonade								
30 min. after glucose	200	25 c.c.	0.3%	133	70 c.c.	0.8%	171	0.9
1 hour after glucose	250	50 c.c.	1.3%	111	200 c.c.	0.3%	135	6.0
2 hours after glucose	190	200 c.c.	0.8%	99	170 c.c.	Trace	107	1.2
3 hours after glucose	124	60 c.c.	0.1%	...	...	.....	...	..

Member 10. White male, aged 60, a son of member 1, weighs 210 pounds (95.5 Kg) and is 5 feet 8 inches (172.7 cm.) tall; a reducing substance has been found in his urine by several physicians over a period of years.

Member 13. White female, aged 13, a daughter of member 6, and a granddaughter of member 1, has a small amount of reducing substance in her urine after a meal.

Member 26. White female, aged 21, a daughter of member 4, and a granddaughter of member 1, was seen Feb. 4, 1925, during the early weeks of her second pregnancy. Sugar had first been found in her urine during the early weeks of her first pregnancy, Oct. 21, 1922; starvation for three days and subsequent restriction of diet had not rendered the urine sugar-free. Her greatest weight had been 115 pounds (52.6 Kg) during 1922. Her average weight was 107 pounds (48.6 Kg). She had never had any symptoms of diabetes. Her height was 5 feet 2 inches (157.5 cm.) and her naked weight was 101 pounds (45.8 Kg). The blood and urine response to glucose, determined March 6, 1925, is shown in Table 2, taken from a report of respiration studies of renal glycosuria by Paullin (9). During the remainder of the second pregnancy, the puerperium, nursing period and subsequently, this patient's glucose excretion was studied and reported by Bowcock and Greene (10). On Nov. 7, 1928, a 24 hour specimen of urine, volume 1200 cc., contained 35 grams of glucose. This patient writes that she is in good health and weighs 109 pounds (50.0 Kg).

Member 27. White female, aged 28, a daughter of member 4, and a granddaughter of member 1, was seen Nov. 7, 1928. The past history was unimportant. She had had no symptoms of diabetes and had had nycturia only during her menstrual periods. Her greatest weight had been 125 pounds (56.8 Kg) 10 years ago; her average weight was 105 pounds (47.7 Kg). I had found 0.1 per cent sugar in a single specimen of urine during November 1926. During June 1927 I examined urine passed two hours after a large meal; this specimen contained 3.0 per cent sugar. The urine was dextrorotary in the polaroscope and was fermented by yeast. Her height was 4 feet 10 inches (147.3 cm.) and her naked weight was 100 pounds (45.5 Kg). Table 3 shows the blood and urine response characteristic of cyclic renal glycosuria following the ingestion of glucose.

Member 29. White female, aged 33, is a daughted of member 9, and a granddaughter of member 1. Her height is 5 feet 2 inches (157.5 cm.) and her weight is 158 pounds (71.8 Kg). On Nov. 17, 1928, a specimen of urine passed after a meal contained a small amount of reducing substance. On Nov. 25, 1928, a postprandial specimen contained 0.43 per cent glucose. The reducing substance reduced Benedict's and Nylander's solutions and gave a heavy yield of osozone crystals with phenylhydrazine.

Member 31. White male, aged 5 years, 6 mos., a son of member 26, and a great grandson of member 1, weighed 6 pounds 4 ounces at birth (2.8 Kg). When one year ten months old, I examined a specimen of his urine which contained 0.1 per cent dextrorotary reducing substance; three subsequent examinations showed a trace of reducing substance on one occasion, and none at the other examinations. On Nov. 9, 1928 he was 3 feet 7½ inches (11.5 Kg). tall, aind weighed 45 pounds (20.5 Kg). A specimen of urine collected two hours after a meal contained 0.23 per cent sugar. The urine gave reduction of Benedict's and Nylander's reagents and yielded an osozone with phenylhydrazine. This child is in good health.

Member 32. White male, aged 3 years, 2 mos., a son of member 26, and a great grandson of member 1, weighed 7 pounds (3.2 Kg) at birth. Except for a mild degree of rickets he has had good health. A specimen of urine at the age of four months gave no reduction of Benedict's solution. On Nov. 9, 1928 his height was 3 feet ½ inch (92.7 cm.) and his weight was 33 pounds (15.0 Kg). A specimen of urine passed two hours after a meal gave slight but definite reduction of Benedict's and Nylander's solutions and a good yield

TABLE 2.—RESPIRATION EXPERIMENTS* MEMBER 26

	Respiratory Quotient	Calories per Hour	Rise in Calories per Hour	Calories per Square Meter per Hour	Rise Above Normal, Per Cent	Calories from Carbohydrate and Fat	Calories from Carbohydrate, Per Cent	Calories from Carbohydrate	Grams Carbohydrate Utilized		Blood Sugar, Mg. per 100 Cc.	Urine Sugar, Gm.
									Total	Increase		
Basal	0.78	55.4	..	37.9	—2	47.1	26.3	12.3	3.0	..	78	+
79 Gm. dextrose 45 minutes after	0.87	62.2	6.8	42.6	16.5	52.8	57.5	30.3	7.6	4.6	133	3.5
1½ hours	0.78	59.7	4.3	40.9	11.0	50.7	26.3	13.4	3.3	.3	132	2.0
2½ hours	0.76	56	0.6	38.4	3.5	47.6	19.2	9.2	2.3	—.7	100	1.5
Dextrose administration											79.0 Gm.	
Dextrose excreted											7.0 Gm.	
											72.0 Gm.	

Dextrose metabolized, 10.5 Gm., 14.6 per cent of total

*Technic as described by Boothby and Sandiford; Tissot gasometer and Haldane gas analysis apparatus. The results demonstrate normal utilization of dextrose.

TABLE 3—GLUCOSE TOLERANCE TEST

Member 27	Blood Sugar in mg. per 100 c.c.	Urine Volume	Urine Sugar
Fasting	89	15 c.c.	Negative
100 grams glucose as lemonade			
20 min. after glucose	131	11 c.c.	1 Plus
40 min. after glucose	134	45 c.c.	3 Plus
1 hour after glucose	122	75 c.c.	3 Plus
2 hours after glucose	105	445 c.c.	2 Plus
3 hours after glucose	83	220 c.c.	1 Plus
Total volume urine containing sugar		796 c.c.	0.38% = 3 gms.

of osozone crystals when treated with phenylhydrazine.

Member 33. White female, aged 12, is a daughter of member 29, and a great granddaughter of member 1. Her height is 4 feet 8½ inches (143.5 cm.) and her weight is 70 pounds (31.8 Kg). At two examinations postprandial specimens of urine have reduced Benedict's and Nylander's solutions and given a good yield of osozone crystals.

Member 34. White female, aged 4, is a daughter of member 29, and a great granddaughter of member 1. Her height is 3 feet 2 inches (96.5 cm.) and her weight is 30 pounds (16.6 Kg). On two occasions her postprandial urine has reduced Benedict's and Nylander's solutions; at one examination the quantitative reduction was 0.29 per cent. A heavy yield of crystals was obtained with phenylhydrazine.

Member 35. White female, aged 7, is a daughter of aglycosuric member 30, (member 30, aged 25, is 5 feet 5½ inches tall and weighs 188½ pounds; a postprandial specimen did not reduce Benedict's solution), and a great granddaughter of member 1. Her height is 4 feet 3 inches (129.5 cm.) and her weight is 52 pounds (23.6 Kg). One of two postprandial specimens gave slight reduction of Benedict's and Nylander's solutions, and a good yield of osozone crystals.

Member 36. White female, aged 5, a sister of member 35, is 3 feet 7 inches tall (109.2 cm.) and weighs 39 pounds (17.7 Kg). Two postprandial urine specimens gave slight reduction of Benedict's and Nylander's solutions and a good yield of osozone crystals.

Member 37. White female, aged 3, a sister of member 35, is 3 feet 2½ inches tall (97.8 cm.) and weighs 35 pounds (15.9 Kg). Two postprandial specimens of urine produced definite reduction of Benedict's and Nylander's solutions and yielded osozone crystals after treatment with phenylhydrazine.

DISCUSSION

In spite of the fact that only one or two postprandial urine specimens from most of the individual members of this family were examined, positive reduction was obtained with the urine of eighteen members. This high percentage of positive results (58 per cent), suggests that had specimens been examined at more frequent in-

tervals the strong hereditary trend of this symptom, glycosuria, would have been evidenced by a still higher percentage of positive results.

As far as could be determined, all members of the family are in comparatively good health, and in none have the classical symptoms of diabetes mellitus been present. The family is remarkable for the fact that it shows no member with typical symptomatic diabetes. The absence of such symptoms, however, does not exclude the presence of mild diabetes, and studies of the blood sugar response to glucose ingestion would probably demonstrate the presence of a mild diabetic type of reaction in some of the asymptomatic adult members besides member 4. The juvenile members have most probably a benign glycosuria. The types of blood sugar and urine response to the ingestion of glucose displayed by the members thus studied, comprise the usual types of reaction noted in such families. There is, in addition to such types, a rarer type of benign glycosuria which may be present in this family. Campbell (11) has described this rare type under the designation of diabetes innocens. The condition is characterized by a low renal threshold, giving rise to the presence of sugar in urine collected simultaneously with a low or normal fasting blood sugar. There are usually no symptoms of diabetes. After food the blood sugar does not exceed the normal postprandial level, while following the ingestion of glucose the blood sugar level increases to the point of a definite hyperglycemia but returns to normal within three hours. No special dietary restriction is necessary for the well-being of such individuals. Vogelenzang (12) has described two such cases which he classifies as a probable combination of diabetes mellitus and renal glycosuria. Parsons (13) has reported a similar case under the title of "benign glycosuria with hyperglycemia." Holst (14) mentions a further case. Malmros (15) records an example in one of the glycosuric families, and Paullin and Bowcock (16) have made a detailed study of a similar case with special threshold studies in a patient who was unaware of any other cases of glycosuria in his family.

Whether or not any of the members of this family will subsequently develop symptomatic diabetes is problematical. Holst (3) and many others are of the opinion that a transition from benign non-diabetic glycosuria to true diabetes seldom, if ever, occurs. Malmros (17) after studying the reaction of such glycosuric individuals to insulin and noting that although they developed hypoglycemic symptoms, they did not become sugar-free, concluded that an insufficiency of the pancreas does not cause these forms of glycosuria.

Summary

A family is reported, eighteen members of which (representing 58 per cent of the members studied) displayed the presence of a reducing substance in the urine in the absence of other symptoms of diabetes. Glycosuria was first discovered at 22 months in the youngest, and at 78 years in the oldest member. The condition is present in four generations. The blood and urine

response to glucose ingestion has been determined in five members, showing the responses characteristic of mild diabetes mellitus in one case, of cyclic renal glycosuria in two cases, and of renal glycosuria in two cases.

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A Study of Atrophic Cirrhosis of the Liver in Relationship to Syphilis*

By Don M. LeDuc, *Ann Arbor, Michigan*

This paper comprises a review of all cases of cirrhosis of the liver which have occurred in the pathology service of the University of Michigan from the year 1895 through the major part of the year 1925, with the exception of all cases of central cirrhosis, biliary cirrhosis, fatty cirrhosis, and four cases that could not be definitely classified. Special emphasis is placed upon the concomitant presence of histological evidence of syphilis, either in the liver, or elsewhere in the body.

An exhaustive resumé of the literature was not attempted. Cirrhosis of the liver was described as a hardening of the liver by Vesalius (1514-1564), Harvey, and Morgagni (1). Payne's review (2) of the history of cirrhosis of the liver points out that the earlier workers attributed its cause to the over consumption of water and the excessive use of spirituous liquors among other things. Modern opinion tends to center about two foci. Hawkins (3) would have us believe that atrophic cirrhosis of the liver has no direct etiological relationship to syphilis. He admits that there may be an indirect, or parasyphilitic relationship, but favors chronic alcoholism as the causative agent. Symmers (4) is equally emphatic in his belief that alcohol plays but a minor rôle in the etiology of atrophic cirrhosis, and that there is at least a certain group of cases of atrophic cirrhosis of the liver in which syphilis is a primary factor. To further minimize the importance of alcohol Symmers states that atrophic cirrhosis of the liver is equally common in Brahmins and Mohammedans, among whom the use of alcohol is religiously forbidden, and further, that the long continued administration of alcohol to experimental animals has at no time resulted in the production of atrophic cirrhosis. In a few cases (5) a condition similar to atrophic cirrhosis has been produced in experimental animals by the continued use of sclerotic poisons, such as chloroform, in conjunction with certain microorganisms and their toxins. One would expect, if Hawkins is correct, that in known chronic alcoholics the incidence of atrophic cirrhosis would be relatively high as compared with all cases of atrophic cirrhosis. This fact is

*From the Pathological Laboratory, University of Michigan, Ann Arbor, Michigan.

largely mitigated by the findings of Symmers (4) and Formad (6). The former found but 3% of cases of atrophic cirrhosis among all autopsies performed on known chronic alcoholics, and the latter found but 6 cases of atrophic cirrhosis among 250 alcoholic patients that came to autopsy.

In studying our cases no attempt has been made to observe the incidence of chronic alcoholism for the reasons that this service includes people from all walks of life, and that many of the histories are too meager in this regard.

With the above exceptions the 2285 autopsies contain 58 cases of atrophic cirrhosis, 16 cases of early cirrhosis which generally have the characteristics suggestive of early atrophic or early syphilitic cirrhosis, 19 cases of syphilitic cirrhosis, and 8 cases of Glissonian cirrhosis.

Type	No. of Cases	Percentage
Atrophic	58	.0253
Syphilitic	19	.0083
Early	16	.0070
Glissonian	8	.0035

Atrophic Cirrhosis

In our series of 2285 autopsies atrophic cirrhosis was diagnosed 58 times or 2.5%. This is somewhat higher than the results found by Symmers at Bellevue Hospital, 1.7%. His percentage is based on 4880 autopsies. The 58 cases may be tabulated as follows:

Total No. Cases of Atrophic Cirrhosis.. 58
No. of Cases of Atrophic Cirrhosis Associated with Histological Lesions of Syphilis 34
Average Age—53 yrs.
Males 29
Average Age—53.8 yrs.
Females 5
Average Age—48.4 yrs.
No. of Cases of Atrophic Cirrhosis not Associated with Lesions of Syphilis.. 24
Average Age—44.6 yrs.
Males 15
Average Age—43.2 yrs.
Females 9
Average Age—46.6 yrs.

Symmers observed the histological lesions of syphilis in 24 of 84 cases of atrophic cirrhosis, 28.3%. We find this association to be much higher, 34 in 58 cases, 60.3%. The age incidence is seen to run somewhat higher where syphilitic lesions are also present.

In the 34 cases of atrophic cirrhosis associated with syphilis in our series the distribution of cellular evidence of syphilis is as follows:

Lesion	No. of Cases	Percentage
Syphilitic Aortitis*	30*	88.2%
" Orchitis	16	47.0%
" Myocarditis	16	47.0%
" Pancreatitis	12	35.2%
" Adrenalitis	12	35.2%
" Hepatitis	9	26.7%
" Leptomeningitis	5	14.7%

*Lesions occurring less than five times are not recorded.

Syphilitic Cirrhosis

The average age incidence for the 19 cases in this group was found to be 41.1 years. The 12 males averaged 33.8 years which is considerably below the average of 43.9 years for the 7 females. As in atrophic cirrhosis associated with syphilis the incidence of other lesions of syphilis is marked, but considerable lower.

Lesion	No. of Cases	Percentage
Syphilitic Aortitis	8	42.1%
" Myocarditis	7	36.8%
" Adrenalitis	7	36.8%
" Orchitis	6	31.5%
Hepar Lobatum	6	31.5%
Syphilitic Pancreatitis	5	26.3%

Early Cirrhosis

As previously stated cases placed in this group, while they favored either the atrophic or syphilitic groups, were too insufficiently developed for positive classification. There were 16 cases. Only one, a male aged 76 years, showed no histological evidence of syphilis. The average age of the 15 syphilitics was 50.6 years, that of the 7 females was slightly more than half (37.6 yrs.) that of the 8 males 60.3 yrs.). Lesions of syphilis were present as below:

Lesion	No. of Cases	Percentage
Syphilitic Aortitis	10	66.6%
" Myocarditis	9	60.6%
" Pancreatitis	8	53.3%
" Adrenalitis	6	40.0%
" Orchitis	6	40.0%
" Leptomeningitis	5	33.3%

Glissonian Cirrhosis

Of the 8 clear cut cases of this type of cirrhosis half are found in syphilitics. The average age is 26.5 years. The 3 females average 39 years and the 5 males average 17.2 years. The syphilitic lesions were found in two babies and two middle-aged adults. Old syphilitic lesions occurred in one case, orchitis syphilitica fibrosa in another, and congenital syphilis in the two babies.

Discussion and Conclusions

If we combine the results of atrophic cirrhosis and early cirrhosis we find:

Total No. of Cases	Associated with Syphilis		Not Associated with Syphilis	
	Cases	Percentage	Cases	Percentage
74	49	66.6%	25	33.7%

Going a step farther and combining all four types we see:

Total No. of Cases	Associated with Syphilis		Not Associated with Syphilis	
	Cases	Percentage	Cases	Percentage
101	72	71.2%	29	28.7%

It would seem from the material available in this service that atrophic cirrhosis of the liver is relatively common, and that its relationship to syphilis is more pronounced than in other services.

If the syphilitic type of atrophic cirrhosis may be properly combined with the early cirrhotic type, the incidence of concomitant lesions of syphilis increases, and if all four types may be combined the incidence swells enormously.

The low frequency with which other observers associate atrophic cirrhosis and syphilis may be partly explained upon the relative infrequency with which they diagnose visceral syphilis.

The lack of sufficient data prevents one from being more dogmatic in this matter, but certainly the frequency with which one finds well marked lesions of syphilis so constantly present in such a large percentage of cases of atrophic cirrhosis is of significance.

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Focal Calcification of Heart Muscle; Case Report

By Vincent De Paul King, M.D., *Memphis, Tennessee*

CALCIUM may be deposited within the cardiac tissue or precipitated directly into the endocardium. Healthy tissue never shows calcium salts deposited. Deposition of the calcium salts in dead or deteriorated tissue, however, is not very uncommon. (1) At first the process consists of a deposition of fine calcium granules, usually phosphates, within the broken up heart muscle fibers. These calcium granules may then coalesce, forming plaques, the latter gradually involving all elements of the heart substance. Scholtz (2) points out that there is no specific cause for this condition but that calcification can occur in the course of any pathological condition, which gradually leads to degeneration of the cardiac muscle fibers of diffuse or localized type. It has not yet been discovered just what rôle pathological conditions of the kidneys plays with respect to its causing interference with calcium excretion and thereby probably increase in the total amount of free calcium salts, aiding the production of pathological calcification such as occurs in the myocardium.

It is the opinion of investigators along this line that the ultimate cause of pathological calcium deposition seems to lie in factors controlling the calcium tolerance of the cell and in the character of the physio-chemical processes within the individual cells.

Calcium precipitation is an extremely rare condition, and the only two cases which have been reported involved the endocardium only. In both cases the condition was observed in association with calcium metastasis. By metastatic calcification is meant the direct precipitation into apparently normal tissue of the overload of circulating calcium salts produced by extensive bone destruction within the body. The precipitated calcium salts in such cases are occasionally found in the auricles of the heart (also in kidneys, stomach, and lungs). Here too, the endocardium of either right or left auricle is involved. Calcium metastasis could be considered a clinical entity composed of a clinical picture of primary bone destruction, finally superimposed by a second clinical picture somewhat suggestive of acute rheumatism. The real underlying causes of calcium metastasis are still unknown. However, the theory which seems plausible is the main causative factors consist of over-saturation of the circulation with calcium salts associated later on with a breakdown of the mechanism normally provided for excretion of calcium salts.

followed eventually by precipitation of the calcium overload in the places mentioned above.

Calcium deposition in the myocardium has been shown by Diemer, Oberndorfer, MacFarland, and Lucas to be the result of extension of the process from the overlying pericardium.

A few remarks on pericarditis calculosa, so-called, or concretio pericarditis, may, therefore, be made here. A review of the literature up to 1923 by Case (3) shows that in only 13 instances has this been recognized in life. Cutler and Sosman (4) have recognized similar calcification in three patients with chronic heart disease.

In one case, the endocardium, pericardium, and myocardium were all involved.

Wells (5) found 4 cases of similar type (pericarditis calculosa) out of 128 cases of pericardial adhesions from a total 1,000 autopsies.

Calcium deposits in the bundle of His has been reported by Waldorp (6) (1924).

Calcification of the heart may be demonstrated intravitam if extensive enough. In such instances one may even succeed in differentiating it from pericardial calcification. Small calcium foci, however, cannot be demonstrated by X-ray during life. Small fine solitary calcium foci within the heart wall may be sometimes overlooked at necropsy, as in case herein reported. This may be avoided to some extent by taking X-rays of the removed autopsy specimens whereby very fine calcified areas are localized. Such autopsy radiographic work if carried on systematically will show that the myocardial calcification is not so very rare as is believed.

X-ray is a very important aid for pathologists in research for small calcium foci and for other changes which cause radio-graphically sufficient differences of tissue density.

Cardiac degeneration due to obliteration of the coronaries with associated calcium deposition have been reported by Burns, Askanazy, and Scholtz (7). Coats and Hedinger described cases (one each) in which myocarditis was due to sepsis. Weichert reported a similar case in which the myocardial damages in which the calcium deposits were found were due to sepsis. Tily described a case of bichloride poisoning resulting in myocardial changes associated with calcification of the heart muscle.

Two cases, one by Roth and another by Siebenmann, have been reported in which there was a combination of metastatic calcification and that due to or associated with myocarditis.

Case Report

W. L., colored male, age 47, was admitted to the Memphis General Hospital October 27, 1926 at the request of the Social Service Bureau. As the patient was in the state of coma, it was impossible to get a reliable history. However, there was no knowledge of any previous illness until three weeks before the entrance, when his feet and ankles began to swell.

Physical examination showed heart apex 3 cm. outside ant. ax. line. Systolic murmur at the apex and short diastolic murmur down the left sternal border. At the bases of the lungs there were coarse and fine râles with unimpaired resonances.

There was marked edema of the subcutaneous tissue.

Blood pressure 190/150, Temperature 98°, pulse 90.

Blood N. P. N. 162.5; Creatinine 5.68; Uric acid 8:42.

Total leukocytes—9,450, P. N. 88% L. 10%, L.M. 11%.

Total erythrocytes—3,590,000. Hb—70% (sahli).

The Wassermann test was negative.

The urine contained slight trace of albumin and a few red cells.

The clinical diagnosis was Malignant Hypertension; Myocardial Insufficiency; Uremic Coma.

Treatment:

Blood was removed twice by reinpuncture: October 30, 200 c.c. were drawn, and 400 c.c. of Fischer's solution were given intravenously. On November 2, 300 c.c. of blood were drawn and 500 c.c. of Fischer's given. 1 ampule of digifolin was given every four hours October 28, 29, 30, then discontinued. Patient was given the Karrell diet beginning November 1st.

The temperature during the following week ranged from 95 to 99.6. The pulse ranged from 86-124. On November 2 the blood pressure dropped from 170/120 and practically all of the oedema had disappeared.

On November 3, the blood showed—N.P.N. 246.15; creatinine 7.27 CO_2 42 vol per cent. Sugar 0.148 mg.

On November 6 the patient died without having regained consciousness.

Necropsy

The body was that of a negro male well developed but somewhat emaciated, 174 cm. in length. There was a conjunctivitis, a pyorrhea, alveolaris, and dental caries. There was also a denuded surface on anterior chest wall, scars and wrinkling over both tibiae. Axillary, inguinals and epitrochlear lymph glands were enlarged. A penile scar, and a large denuded surface over the sacrum, obviously a bed sore were present.

Internal Examination

Peritoneal cavity—There were fibrous adhesions between the omentum and liver and omentum and spleen. There was a mucosal ulceration in ileum just above the cecum 2x3 cm. brownish in color and edges smooth, not quite perforating. The liver seemed smaller than normal, firmer and was adherent to anterior chest wall. The spleen was adherent to diaphragm and omentum and seemed smaller and firmer than normal.

Pleural cavities: There were dense fibrous adhesions on the right lung between parietal and visceral pleurae, also between the visceral pleura and pericardium and diaphragm. There were 560 c.c. straw-colored fluid in left pleural cavity. Both lungs were soft and juicy.

Pericardial cavity: There was a fibrinous exudate over the entire pericardial cavity. There were large waxy patches on left ventricle and left auricle. The heart was markedly enlarged, apex reaching to 6th interspace, anterior axillary line.

Heart—Weighed 580 grams. The aortic mitral and tricuspid valves were thickened. There were silvery streaks and yellowish areas in the reddish myocardium. The wall of left ventricle was 2½ c.m. thick.

Aorta: Presented thickened, wrinkled, bark-like appearance.

Lungs: They were soft and juicy on cut surface, serum exuded and cut surfaces presented dark, reddish appearance.

Liver: Weighs 1100 grams. There were dense adhesions. The liver was firmer than normal. There were numerous hard contracted areas throughout. There was a small calcified area on the anterior surface. On cutting the liver was resistant to the knife and presented a reddish color. The gall bladder and ducts were negative.

Spleen: Weighs 11 grams. It was firmer than normal with thickened capsule. It cut with increased resistance, and had a reddish color.

Gastro-intestinal tract: About 4 c.m. above the cecum there was an ulceration 2x3 cm., edges smooth, brownish, necrotic tissue in center. It involved all coats of intestines, but did not perforate.

Kidneys: Right weighed 65 grams. It was small, firm, contracted, and deeply scarred. The capsule was difficult to strip and left a finely granular surface. On cut surface, the cortex was slightly narrowed, and the vessels stood up above the surface, slightly thickened. The left kidney weighed

100 grams; vessels stood up above the surface; cortex not strikingly narrowed.

Brain: Some slight edema; otherwise negative.

Microscopic: Heart section revealed a slight hypertrophy of the myocardium; a rather marked increase of connective tissue. The walls of the blood vessels were thickened. No exudate was seen on the epicardium. There were irregular spotted areas of calcification (see Figure 1).

Pancreas: Section revealed a marked increase of inter- and intralobular connective tissue. Blood vessels thickened.

Kidneys: Section revealed an enormous thickening of the walls of the largest blood vessels. The medium sized blood vessels showed hyperplastic intima. The arterioles were not very markedly thickened. The capillaries were congested and distended with red blood cells. There was marked increase of intertubular connective tissue

FIG. 1. Microscopic section of cardiac muscle showing focal necrosis and calcification.

Lungs: Section revealed marked thickening of the walls of the larger blood vessels. There was chronic passive congestion and some emphysema.

Liver: Section revealed a marked chronic perihepatitis and marked chronic passive congestion.

Spleen: Section revealed marked chronic congestion; a marked thickening of the walls of the larger blood vessels.

and large and small aggregations of small round cells throughout the section. The tubules were atrophied, and there were numerous hyaline casts. Some of the glomeruli appeared normal and others showed increase of the endothelial elements of the glomerular tufts; others showed hyalinization of the glomerular tufts; while still others were atrophied and showed marked fibrosis with

fibrous tissue growing in from the capsule to the glomerular tuft.

Anatomical Diagnosis:

Primary: Malignant hypertension (genuine contracted kidney: sclerosis and nephritis) chronic myocarditis with spotted calcification; syphilitic mesaortitis; chronic passive congestion of thoracic and abdominal viscera; acute fibrinous pericarditis; syphilitic ulcer of the ileum.

Subsidiary: conjunctivitis; dental caries; pyorrhea aleolaris; penile scar.

Cause of death: Malignant hypertension with resulting uremia.

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Status Lymphaticus

By Dr. Henry M. Ray, M.D., *Pittsburgh, Pennsylvania*

THERE is no generally accepted definition of "Status Lymphaticus." This condition clinically is at least in part related to certain constitutional defects variously designated under the terms: laryngismus, asthma thymicum, constitutio lymphaticus, status thymicolymphaticus and others. All of these conditions described at different times by different observers, represent in all likelihood different manifestations and degrees of the same constitutional defect which was first mentioned more than 300 years ago by Felix Plater, who in 1614, reported the sudden death with no apparent cause of a five month's old boy whose most prominent pathologic finding at autopsy was the enlarged thymus. Thus the thymus was made to bear the etiologic burden on the basis of compression of the trachea and adjoining vascular structures and autonomic nerve trunks until the masterful publication in 1858 by Friedleben who established the dictum "Es gibt kein asthma thymicum" and denied that the symptoms were due to pressure. This view was later supported by Paltauf who based his conclusions on a vast amount of pathological material.

Status lymphaticus may be defined as a constitutional defect usually hereditary but occasionally acquired, characterized clinically by definitely peculiar changes in the external configuration, lowered immunity to infection, increased susceptibility to chemical and physical agents and frequently sudden death; physiologically there is an impaired function of the autonomic nervous system, the gonads and adrenals and pathologically, hypoplasia of the cardio-vascular system, arrested development of the chromaffin sysadrenals and pathologically hypoplasia of the lymphoid tissue throughout the body including the lymph follicles of the spleen and hyperplasia or arrested involution of the thymus gland.

Experimental work on status lymphaticus establishes the close interrelation between the thymus and adrenals. In rabbits and rats, suprarenalectomy is followed by rapid regeneration and hyperplasia of the thymus and lymphoblastic tissue. It was first demonstrated by Lewis that removal of the suprarenals in rats reduced their resistance at least 400 times. In fact, it was later shown by Scott, Také and Marine and Jaffe that suprarenalectomy in animals produces greater lowering of resistance and hypersusceptibility than any other known experimental procedure. It is interesting to note that the immunologic response is not impaired in as much as the suprarenalectomized

animals retain their capacity to produce antibodies in spite of their lowered resistance. Thus as observed by Tanabe, cases of status lymphaticus in the Japanese army, while manifesting violent reactions to usual doses of typhoid vaccine showed no impairment in their titre of agglutinin production.

The fact that too much emphasis has in the past been placed on the thymus in the etiological role is responsible for the diversity of opinion in the interpretation of status lymphaticus and indeed as recently as 1927 it was asserted by Greenwood and Wood that the term status lymphaticus is a medical myth. Such an unfortunate assertion appears all the more inconsistent to one who has spent any time in the dead house and observed the constant pathologic anatomy of this condition. Status lymphaticus is certainly a distinct pathological entity and to a certain extent also a distinct clinical entity. The thymus plays only a secondary part in the picture and its size depends on the stage or degree of the lymphoplastic reaction at the time.

A clearer conception of the role of the thymus in this condition is hardly possible until more is known of the physiology of the gland. I have reason to believe that the thymic cells are really lymphocytes and that the gland is essentially a lymphoblastic structure. The thymus increases rapidly in weight to the beginning of the third year, remaining stationary until the seventh year when it increases slightly and declines about the eleventh year. At the age of puberty the gland begins to undergo a progressive involution or atrophy. I am not in accord with the prevalent view that the thymus disappears completely after middle age. In 800 autopsies on individuals past 45 I have observed evidence of glandular remains by histological examination of the anterior mediastinal pad of fat in 20 per cent of subjects, in the majority of whom there was no naked eye evidence of thymic remnants.

That the thymus gland begins its permanent involution with sexual maturity is evidence of the close interrelation with the sex glands as well as the other endocrine structures, notably the thyroid and adrenal. It is interesting to note that during the involutionary stage there is regeneration of reticular cells, thymic cells and Hassall's corpuscles, but regerenation cannot keep pace with the involution process except in pathological involution due to infections, intoxications and X-ray exposure, where regeneration may be rapid and complete.

That the thymus has an internal secretion has not been proved. Rather are most inclined to regard it as a lymphoid structure. It has been experimentally established that thymectomy is not followed by important symptoms and that the organ is in all likelihood not essential to life. Its most important contribution is in the nutrition and growth up to the time of sexual maturity, particularly in the development of the bony system. Thus the outstanding effects of experimental thymectomy are referable to the calcium metabolism and deficient ossification. Some attribute to the gland an ability to form antibodies and a detoxicating function (Barbara).

In the relation to the hemopoietic system the thymus like the other lymphoid structures is an important source of lymphocytes and possibly also of eosinophils. In all likelihood it has no bearing on red cell formation.

Interrelation of the thymus with the glands of internal secretion is seen in the effects of castration, suprarenalectomy and thyroparathyroidectomy. While removal of the sex glands does not stimulate the thymus to growth it certainly inhibits its involution. Removal of the suprarenals not only prevents involution but also stimulates regeneration. The thyroid gland on the other hand appears experimentally to have an opposite effect since thyroidectomy reduces the growth of the thymus and hastens involution.

Pathologically, the picture of active status lymphaticus is a very definite one. The thymus is enlarged and the microscopic picture depends upon the age of the individual. The medulla shows invariably, lymphoid hyperplasia while the cortex may be sclerotic. An eighteen months' old male child upon whom I performed a necropsy following sudden death from violent dyspnea and cyanosis, presented a relatively huge thymus which weighed 86.5 grams. Symmers states that in the large series of necropsies at Bellevue Hospital, the thymus in typical status lymphaticus averaged 25 grams. The spleen is usually enlarged, sometimes palpably so the Malpighian follicles are increased in number and size and endothelial elements are occasionally hyperplastic. While there is no demonstrable enlargement of the superficial regional lymph nodes, the lingual and faucial tonsils and naso-pharyngeal lymphoid tissue are markedly hyperplastic and there is definite hyperplasia of the intra-thoracic and abdominal nodes, Peyer's patches and solitary lymph nodes of the intestine. Collections of lymphoid cells are found in the viscera, particularly the liver. The thyroid is likely to be enlarged and the suprarenal bodies, particularly the medullary substance and extra-glandular chromaffin tissue show hypoplasia. The cardio-vascular system is underdeveloped, the vessels narrow and the walls thin and delicate, lacking elastic tissue and deficient in muscle tissue. Myocardial degeneration, hemorrhages and atheromatosis are prone to supervene. The osseous system shows evidence of impaired calcification and in younger subjects rickets is often associated.

In the recessive types, the thymus has been practically entirely replaced by fat and the hyperplastic lymphoid structures show atrophy with sclerotic changes depending upon the stage of involution. The skeletal changes and body configuration of course remain unmodified.

Clinically, the children are well nourished, gracefully formed, the skin is marble-like and velvety and the hair is fine and silky. In adults too, the skin is pale and delicate, the facial and axillary hairs are scanty, there is very little or no hair on the chest and in the male the abdominal hair is absent and the distribution of the pubic hair resembles that in the female. The thighs are gracefully arched, the waist narrow and external genitalia small. In the female, the usual graceful lines are exaggerated and the

axillae contain fat pads with little or no hair. Most of the cases I have seen in females have been blondes.

There is usually a lymphocytosis, hypotension and hypoglycemia. The coagulation time is prolonged. I have never failed to find the lingual tonsils hypertrophied and this is particularly valuable, as it offers an important sign when one is examining a subject who has had a tonsillectomy.

Children mature slowly and secondary sex characteristics are delayed; the musculature is flabby and there is lack of resistance to fatigue and infection. While sudden death sometimes occurs and dramatically so, most cases are probably well able to withstand traumatism and to overcome infection.

The pathogenesis of status lymphaticus is not clear. The condition is obviously congenital although there is no evidence that it is hereditary. Infections in early life probably play an important part.

The actual cause of death in this condition is by no means clear. Many deny that mechanical pressure of an enlarged thymus can itself be responsible. Schule has shown that it requires a weight of 1000 grams to actually close an infant's trachea. In the baby with the huge thymus whose necropsy I have referred to, the gland covered the entire right heart and was adherent to the pericardium. The anatomic signs were those of asphyxia. It is difficult to ignore not alone the possibility of compression of the vessels and right heart but also the influence, particularly in a stage of acute swelling, on encroachment of the thoracic inlet and the effect of pressure on the vagi and recurrent laryngeal nerves with subsequent spasm of the glottis.

In adults the cause of death must be sought for elsewhere. None of the many expounded theories is in itself acceptable. To state that the condition is a hypersusceptibility to physical and chemical agents is no etiologic elucidation. Some state that it is a constitutional defect with increased vagus tone, insufficient chromaffin tissue and inherent weakness of the sympathetic system. Others, notably Symmers believe that anaphylaxis plays an important part and that sensitization and shock result from the liberation of certain nucleoproteids from the massive and widespread necrosis of the centers of the germinal follicles. It is likely that all of these factors combine to contribute to the final outcome. In the sudden so-called thymic deaths of infants, one is reminded of the pathology in the experimental anaphylactic deaths of animals. I have observed the marked fluidity of the blood, the dilated right heart, the cerebral edema with scattered minute brain hemorrhages, the congestion of the viscera especially the lungs and the petechial hemorrhages of the visceral pleura, epicardium and peritoneum. In adult subjects, the majority of deaths are due to the failure of the inherently weak cardiovascular system. Thus in a number of necropsies on steel mill workers, six of which manifested anatomic signs of status lymphaticus, five showed degenerative myocardial changes with cardiac dilatation and one a thirty-two year old Lithuanian, died suddenly with rupture of a small aneurysm

of the anterior communicating artery of the circle of Willis. The hypoadrenal state is known experimentally to increase the susceptibility to shock and infection and in its relation to the effect on disturbing the harmonious balance of the endocrine system with the frequently resulting hypoglycemia which occurs in the human subject of this disease, one must consider an existing autonomic imbalance with inevitable disturbance of the metabolism.

Medicolegal Considerations—Great importance attaches to status lymphaticus in legal medicine, particularly in the matter of sudden death. This was first recognized by the Vienna school of pathologists, notably by Paltauf and Kolisko. Among 5652 autopsies in Bellevue Hospital, Symmers recognized 457 cases of which most were active, some recessive and others partial. It must be remembered that in later years the thymus and lymphoid tissues atrophy. In a review of 2012 necropsies of my own I find recorded in the anatomic diagnosis, status lymphaticus either active or recessive, 180 times. It is to be noted that status lymphaticus will be more often recorded in a series of necropsies in a medical examiner's or coroner's service than in a routine hospital postmortem service, in virtue of the fact that the former is more likely to deal with cases of sudden death and suicides. Many of the subjects of status are mentally deficient and manifest evidence of nervous and mental disease. Thus Bartels observed in an analysis of 122 cases of suicide, that anatomic evidence of status was constantly present. Ohlmacher found definite signs of status in the great majority of fatal cases of epilepsy.

In infancy, many cases of sudden and unexpected death terminating with rapidly increasing dyspnea or cardiac failure, reveal at autopsy that the thymus is much enlarged and the evidence is not altogether conclusive that death can be attributed solely to mechanical pressure on the trachea or great vessels. In adult life, death is more frequently referable to the complications following the hypoplasia of the cardiovascular system. The small heart and narrow aorta with the delicately thin vessel walls are subject to functional disorders, inflammatory lesions, aneurysmal dilation and rupture. Thus we have the sudden and unusual deaths in bathers, or after insignificant trauma or following the careless administration of foreign protein or other substances intravenously. Necropsy records show that a large proportion of rapidly fatal cases of infectious diseases are subjects of status lymphaticus. Subjects with generalized Hodgkins disease usually show anatomic signs of status and many of the endocrinopathies are associated with status in various ways. Hypoplasia of the genitals is common and the bodily configuration has many of the features of pituitary adiposogenital dystrophy.

The case of the young chorus girl, twenty-one years old is an example of the marked hypoplastic state of the vessels in this condition and emphasizes the importance of status lymphaticus in legal medicine. It appears that this girl while walking with an escort, engaged in an argument, whereupon he pushed her vehemently

and she fell to the side-walk, becoming unconscious and dying before the arrival of medical aid. The necropsy of this beautiful blonde, showed the smooth pale marble-like skin, silky hair, total absence of body hair except a scanty amount over the pubes and very little over the two distinct fatty axillary pads. The breasts were small, the waist extremely narrow and the pelvis extremely wide with flaring ilia and gracefully arched thighs. The lymphoid tissue was everywhere hyperplastic, the thymus weighed 24.5 grams, the spleen was enlarged and presented huge Malpighian follicles which showed histologically, necrotic centers. Peyer's patches were large thickened swollen masses of lymphoid tissue and the solitary follicles were prominent. The adrenals were small and showed intramedullary hemorrhagic infiltration. The heart was unusually small, the myocardium flabby and the aorta was thin, inelastic and actually no larger in caliber than the small finger. The vessels at the base of the brain were collapsed, narrow, actually the thickness of tissue paper and upon immersion in water it was interesting to see multiple small thin walled aneurysmal sacs, one of which had ruptured with fatal hemorrhage.

Summary and Clinical Significance—It has been the purpose of this paper to bring out the practical clinical aspects of status lymphaticus. Only too often one hears expressions from apparently scientific clinicians, to the effect that status lymphaticus does not exist in fact and that the term is used by many, mostly pathologists and occasionally clinicians, to mask their ignorance in certain clinical states and more particularly in ascribing to it the cause of death where the actual cause is otherwise obscure. It has been my experience that such expressions emanate from men who rarely, if ever, visit the postmortem room. Such unfounded opinions are easily impressed upon the minds of the younger clinical associates. While most of our younger men are well trained in the practical aspects of clinical laboratory procedure, it is extremely difficult to detect any active interest in postmortem activities. The average interne breathes a sigh of relief after he has completed his attendance at the compulsory number of necropsies. Many a postmortem is performed with only the pathologist and the pathological intern present and this in spite of the fact that the necropsy is announced and advertised on the bulletin board several hours before the postmortem is undertaken. It should be the duty of the chiefs of service to set an example by attending all postmortems and thereby stimulating the proper scientific attitude and habits of the younger men.

There is another group of clinicians who while recognizing the pathological status of this condition, express the opinion that status lymphaticus is entirely a pathological entity and can never be recognized during life. When one observes these cases on the postmortem table again and again, the constant pathologic findings are so pathognomonic as to make an indelible impression. With a visual picture of the anatomic defects and pathological changes in these subjects and keeping in mind those outwardly discernible characteristics already

enumerated, the changes in skin texture, the configuration, the lymphoid hyperplasia (as for example the tonsils and more particularly the lingual tonsils) that can be detected by thorough inspection, the hypotension, the aften associated though slight mental peculiarities, the relative lymphocytosis, the hypocalcemia, the hypoglycemia, a possible history of rickets in early life, the susceptibility to repeated infection, etc., the clinical recognition is no longer a difficult task.

Most of the cases do not die from trivial traumatisms or minor operations and in fact this is a rare occurrence. By far, most of them attain maturity and as time goes on, present certain symptoms which can in part at least be explained by the inherent constitutional hypoplastic state. When the clinician has all these facts in mind, he does not fail to look for these anatomic signs; he studies the cardio-vascular response; he studies the blood count and blood chemical values with particular reference to sugar and calcium; he orders a metabolism determination and makes other clinical tests to detect any pathological change in the endocrine physiology, as for example, the adrenal response with the Goetsch test. Knowing the tendency toward cardio-vascular hypoplasia, he can caution the subject against undue physical or emotional stress productive of sudden blood pressure changes which are unsafe for a delicate thin walled vascular system. The data enables him to advise X-ray therapy, calcium administration, dietary considerations, and certain endocrine products to fit the individual case, as for example, parathyroid, thyroid, pituitary, adrenal substance or sex glands either singly or in combination,

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Two Cases of Cardiovascular Anomaly*

I. Vegetative Pulmonary Endarteritis Complicating Persistent Ductus, II. Hypoplasia of Aorta.

By Newell W. Philpott, M.D., C. M., *Chicago, Illinois*

STUDY of congenital cardiac disease offers much of interest and constantly affords many fascinating problems. It is a well established fact that congenital cardiac defects act as a predisposing factor in the occurrence of infectious heart disease. Cardiac anomalies, especially those of the non-cyanotic group, such as defects in the interventricular septum, bicuspid semilunar valves, and patent ductus arteriosus are commonly the site of infective processes. In a series of 656 cardiac anomalies collected by Abbott the total incidence of inflammatory heart disease was 129 cases, or 19.6 per cent, of which 96 cases were in the non-cyanotic group and 39 in the cyanotic group. The first case which is now being discussed is classified in the non-cyanotic group and is complicated by inflammatory heart disease.

Case No. 1

Our first case illustrates clearly the condition of vegetative pulmonary endarteritis in association with a persistent ductus Botalli and superimposed upon an already damaged vessel wall. The literature records twenty-three cases of patent ductus arteriosus complicated by an infective endarteritis, situated at the pulmonary opening of the ductus and in the adjacent portions of the pulmonary artery. Of these, twenty show an accompanying valvular endocarditis affecting one or more of the heart valves. In only three (Krzyszkowski, 1902; Hamilton and Abbott, 1914; Schlaepfer, 1926) were the heart valves intact with the inflammatory process restricted to the pulmonary artery and the ductus arteriosus. This present case makes the fourth on record of this rare condition.

Report of Case

G. G., aged 6. Weight 33¾ lbs. Admitted to the University Hospital 1/24/28.

Complaints: Mother states that the child has a bad heart and is in a general run-down condition.

Present Illness: The mother dates the illness from July 1927 when the child developed a running right ear. It was thought that this might be complicated by a mastoiditis but the condition was arrested and was cleared up without an operation. The tonsils and adenoids were removed one month later, August 1927. Due to constant fatigue, anorexia, and loss in weight she was kept from school, starting early in October. In the latter part of the same month she developed broncho-pneumonia. Early in

*From the Pathological Laboratory of the University of Michigan, Ann Arbor.

No. 1. Heart opened to expose the aorta and pulmonary artery. A. Aortic cusps. D. Opening of widely patent ductus of Botalli at aortic end. P. First part of pulmonary artery showing very marked vegetations in the lumen above the cusps. Note. The aortic cusps, aorta, and opening of the ductus at the aortic end are absolutely free from any infective process.

November the family doctor informed the parents that the child had a heart condition. For two months previous to admission the child had a hacking cough and lost 7½ lbs. in weight. Abdominal distention also gradually developed.

Personal History: Child was a full term baby. Delivery was normal, the color and respirations did not appear out of the ordinary. Two years ago, 1925, had measles and chicken pox. The family doctor states that for the past two years the child has had frequent, severe attacks of tonsillitis.

Family History: Father and mother are both well. The other two children are in excellent health. The mother's blood Wasserman is negative on two occasions. The other members have not been tested. None in the family have been treated for blood disease.

Physical Examination: The patient is an acutely sick child who gives the appearance of having been ill for some time, and of having lost considerable weight.

Positive Findings: There are many râles at both lung bases. Pulse rate is 160 per minute. There is a marked enlargement of the heart to the left and a slight enlargement to the right. The left border is in the anterior axillary line. There is a diffuse pulsation over the apical and pulmonary areas. The sounds are rapid and regular throughout. A very loud murmur, systolic in time, is heard best in the second interspace to the left of the sternum. This is transmitted laterally to the axilla and up the vessels on the left side. The abdomen is distended and tympanitic. The spleen is markedly enlarged with the lower border two finger breadths below the umbilicus. Liver edge descends four cms. below the costal margin. Some tenderness is noted over the abdomen, but the child appears generally hypersensitive.

Laboratory Findings: The urine shows albumin four plus, many casts, a large number of W.B.C., which are mostly lymphocytes, and an occasional R.B.C. The blood hgb. is 34%, R.B.C. are 3,400,000, W.B.C. are 17,300 of which 72% are polymorphs. CO_2 combining power is 28.7%. Blood Wasserman is 4 plus, repeat 2 plus, and 4 plus on a third test. Blood culture report is hemolytic streptococci. X-ray reports an area in the second interspace on the left of increased density suggestive of tuberculosis.

Course: Was rapidly down-hill. During her stay in hospital she ran an irregular temperature which gradually became higher and before death reached a peak of 106 degrees. Her pulse raised in direct proportion to her temperature, ranging from 120 to 180 per minute. The respirations gradually became more rapid and death occurred six days after admission on 1/30/28.

Final Clinical Diagnosis: Septicemia. Congenital syphilis. Endocarditis and pericarditis. Congenital heart (patent ductus arteriosus?) Subacute glomerular nephritis. Secondary anemia. Abscesses in spleen and liver.

The autopsy was performed five hours after death at 9:30 A.M. 1/30/28.

PROTOCOL (ABRIDGED)

G. G. Aged 6.

External Examination: Body is that of a female child 111 cms. in length. Has a very slight bony frame, and is of the asthenic type. Gives evidence of recent loss in weight. Pupils are dilated with the left larger than the right. The thorax is long and narrow with the intercostal angle much less than a right angle. The abdomen is rounded, boardlike to the touch, with a slight bulging of both flanks. The skin is white and free from ulceration or inflammation. There is no clubbing of the fingers or toes. The incisor teeth have saw-like edges similar to the Hutchinson type. Mucous membranes are pale and slightly cyanotic. Edema is present in each ankle region only. There is a thin white coating over the tongue. The hard palate is high and arched. Ears appear normal with no discharge from either side.

Abdominal Cavity: Contains 175 c.c. of a definitely purulent fluid which contains many fibrin threads. There are many recent adhesions between the coils of small and large bowel. There is no obstruction to the lumen of the bowel. The omentum is thickened and bound down in every portion by

adhesions which tear easily. Liver is 8 cms. below the ensiform and 5½ cms. below the costal border in the right midclavicular line. Spleen extends obliquely below the left costal border for a distance of 7 cms.

Thoracic Cavity: Left pleural cavity contains 100 c.c. of thick, yellow, purulent fluid. There are many adhesions from the posterior surface to the thoracic wall. The right pleural cavity contains 30 c.c. of a turbid fluid which is slightly blood tinged. No adhesions are present on this side. Heart lies transversely in the thoracic cavity, and is definitely enlarged. The apex is behind the 5th rib in the anterior axillary line. The right border is 2 cms. to the right of the mid-sternal line. Left lung is collapsed with the lung borders 7 cm. apart in the anterior mediastinum. A small amount of thymic tissue is present in the anterior mediastinum.

Pericardium: There is a slight increase in thickness toward the base. The tension is definitely increased. The sac contains 50 c.c. of a clear, yellow fluid.

Heart: Measures 9 x 7 x 3½, weighs 180 gms. Is much larger than the cadaver's right fist. All the cavities contain a large amount of cruor. The apex is formed chiefly by the left ventricle which is in firm rigor. There is an occasional subserous petechial hemorrhage toward the base. On opening the aorta it is noted that the ductus arteriosus is patent with an opening in the arch measuring 4 mm. in diameter. It will admit a large probe with ease and the total length is .75 cm.

Right Heart: Left ventricular wall measures 15 mm., and appears markedly hypertrophied. Musculature is light brown with small whitish areas about 2 mm. in diameter noted throughout. The endocardium is smooth and shining with exception of the portion in the left auricular appendage corresponding to the attachment of a parietal thrombus. The mitral valve admits the index finger. The cusps are not roughened and appear normal. The aortic valve admits the thumb. No evidence of vegetations or roughening of the cusps is present.

Right Heart: The right ventricular wall measures 7 mm. and also appears hypertrophied. The musculature resembles that found on the left side. The endocardium is smooth and shining throughout. The tricuspid valve admits 2 fingers with difficulty. The cusps show no gross pathological lesion. The pulmonary valve admits the thumb with difficulty, the cusps appear normal. The foramen ovale is closed.

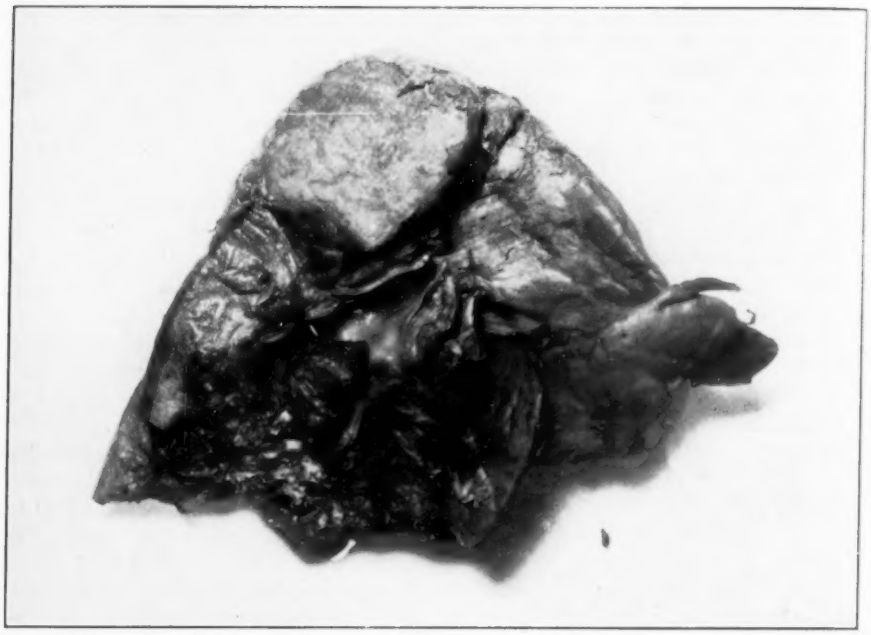
Coronary Vessels: Are patent and appear normal throughout.

Left Lung: Measures 12 x 10 x 3½ cm., and weight 190 gms. The surface is roughened corresponding to the attachment of the adhesions, and there is a marked thickening of the pleura. The lung is atelectatic throughout. Cut section shows many firm, dark areas raised above the surface which appear to be patches of pneumonia. There is a definite increase of fibrous tissue surrounding the smaller bronchi and bronchioles. The smaller branches of the pulmonary artery, more marked in the lower lobe, show many thrombi of different ages; some are organized while others are of a more recent nature. In some portions the vessel wall shows an aneurysmic dilatation. Many corresponding infarcted areas are present, some of which appear secondarily infected. No tubercles are found.

Right Lung: Measures 14 x 13 x 4 cm., weighs 200 gms. The surface is smooth. Many pneumonic and infarcted areas are also noted on this side especially in the lower lobe. There are also many fibrous bands radiating from the smaller bronchi and bronchioles.

Pulmonary Vessels: The opening of the ductus arteriosus is 2 cms. from the superior border of the pumonary cusps. On the inferior and lateral wall 1½ cm., from the pulmonary cusps an area, 3-2 cm., is covered by cauliflower vegetations. These are adherent to the vessel wall and project into the lumen, causing a partial obstruction. The opening of the ductus is situated on the opposite side on the superior and lateral aspect.

Thoracic Aorta: Is normal in size. The intima appears normal throughout. From the opening of the ductus in the arch there is a freshly formed blood clot extending into the lumen of the aorta.



No. 2. Left lung with pulmonary artery exposed. Note the large, round thrombus in the lumen with a definite saccular aneurysmic dilatation of the vessel at the corresponding point of attachment.

No. 3. Small branch of pulmonary artery in right lung completely obliterated by an infected thrombus.

Left Kidney: Measures 10 x 5 x 3½ cm., weighs 130 gms. The fibrous capsule strips with ease displaying a markedly congested surface which is smooth. Cut section gives a distinctly boiled appearance with the cortex raised above the surface of the medulla. The pelvis is not distended and there is no gross evidence of a pyelitis. No infarcts are noted.

Right Kidney: Measures 11 x 4 x 3 cm., weighs 140 gms. Resembles the left in its gross appearance.

Female Genitalia: Shows a normal development.

Microscopic Findings

Cord: Shows early syphilitic meningitis.

Heart: Subepicardial fat shows serous atrophy. Heart muscle is well developed for age, but there is a degenerative fatty infiltration. Endocardium is thickened but there is a degenerative fatty infiltration. Endocardium is thickened, but there is no fresh process. Valvular endocardium is thickened but there are no vegetations.

Aorta: Over the base there is a proliferative pericarditis. Higher in the aorta, at the isthmus, there are definite evidences of syphilis, the lesions being of some standing,—perivascular infiltrations and fibrosis with sclerosis of the media and intima and an older thrombosis on the wall.

Pulmonary Artery: The wall of the ductus arteriosus and of the pulmonary artery shows definite old syphilitic lesions with a superimposed acute streptococcus viridans vegetative endarteritis, with ulceration of the wall and the formation of a mycotic aneurysm, filled with an infected thrombus—thrombo-endarteritis purulenta.

Lungs: Show chronic purulent pleuritis with fibrosis of the pleura. There is a chronic pleuro-pneumonia with marked fibrosis of the interlobular septa. Atelectasis is alternated with dilated air-sacs. Large areas of fibrosis are present. There is a chronic purulent bronchitis. All the branches of the pulmonary arteries show an old obliterating endarteritis with thrombosis. On the older parietal thrombosis there is a secondary vegetative process with a distinct tendency to suppuration, and to the development of mycotic aneurysm. Through the lung are numerous hemorrhagic infarcts in various stages.

Diaphragm: Shows on pleural side an empyema, on the peritoneal side a subacute peritonitis of less degree.

Spleen: There is an extreme congestion with necrosis of the centers of many of the follicles.

Gastro-intestinal Tract: There is a proliferative subacute peritonitis. Mucosa shows an atrophic catarrh.

Pancreas: Shows atrophy but no signs of syphilis.

Liver: Is a typical nutmeg liver with a localized chronic perihepatitis. There is no evidence of syphilis.

Kidneys: Show a sub-acute glomerulotubular nephritis. Many glomeruli are in various stages of repair.

All Lymph-nodes: Show hyperplasia with proliferation of the reticulo-endothelium, There are no tubercles.

Pathological Diagnosis: Mycotic aneurysm of the pulmonary artery opposite the mouth of the patent ductus Botalli (streptococcus viridans infection on an old syphilitic arteritis). Multiple organizing emboli in pulmonary arterial branches with hemorrhagic infarctions. Chronic pleuropneumonia. Atelectasis. Bronchopneumonia. Subacute empyema. Acute syphilitic meningitis of cord. Marked chronic passive congestion of liver and spleen. Sub-acute glomerulotubular nephritis. Diffuse proliferative peritonitis. Marked hyperplastic lymphadenitis.

Discussion

Clinical Findings: From the clinical aspect this case demonstrates very well the condition of persistent ductus Botalli being complicated by an infective process. Before the onset of the fatal illness the child displayed no

definite signs of a congenital heart lesion though she always appeared weak and pale. The last illness was preceded by frequent attacks of tonsillitis, a right-sided otitis media with a questionable involvement of the mastoid region. Other cases on record give histories of a very similar nature. Four have histories of a preceding rheumatic fever; repeated attacks of sore throat were a feature in the case reported by Sommer; Schlaepfer's report states that the onset of the fatal illness was preceded by a bilateral otitis media.

A review of the other cases on record show the physical findings to have a striking likeness. Diagnosis of the patent ductus is made by some or all of the following signs being present:—

1—A thrill felt over the pulmonic area.

2—Dullness in the upper spaces to the left of the sternum.

3—Roentgenray reveals an area of increased density due to increased volume of the pulmonary artery. This is shown in the 2nd left interspace.

4—Accentuated pulmonary second sound.

5—A murmur heard best in the pulmonic area and transmitted up and to the left.

Our case shows:—

1—A diffuse pulsation in the pulmonic and apical regions.

2—Enlargement of the heart to the left.

3—Pulmonic second sound markedly accentuated.

4—Systolic murmur in the pulmonic area and transmitted up and to the left.

The infective process is of a subacute nature, the course being progressively downwards. The average duration is from six months to one year. Two cases, Buchwald and Hamilton, lasted only two months while that reported by Boldero extended over a period of two years. The picture is that of a typical blood-stream infection; blood cultures have shown streptococcus viridans, staphylococcus albus, influenza bacillus, and pneumococcus. The present case proved by blood cultures taken before death and at autopsy to be a streptococcus viridans infection.

Pathological Findings: The picture is typically that of a streptococcus viridans infection superimposed upon an active congenital syphilis. The lungs and pulmonary artery show old syphilitic lesions. Due to lowered resistance and mechanical strain, a vegetative endarteritis developed upon the intima of an already damaged pulmonary artery and ductus. The lungs contain multiple infarcts, abscesses, and areas of chronic pneumonia with an extensive empyema. A secondary peritonitis is present due to an inflammatory extension of the empyema through the diaphragm. The glomerulo-tubular nephritis is typical of that found in streptococcus viridans infections.

There is a definite localization of the vegetative endarteritis to an area in the pulmonary artery opposite the ductus opening and to the ductus wall. The three other cases on record show a very similar localization; those by Schlaepfer and Krzyszkowski have the process strictly confined to that portion of the pulmonary artery at

the ductus arteriosus opening. Hamilton's case shows the pulmonary artery likewise involved but, in addition, the process extends along the wall of the ductus.

Infarcts in the lungs, spleen, kidneys, intestines, skin, and brain are found to be frequent complications. Multiple abscesses in the lungs are common. Thrombus formations in the smaller branches of the pulmonary artery with aneurysmic dilatations of the vessels, similar to those found in the present case, have been reported by Sachs, Kidd, and Krzyszkowski.

This case also demonstrates the fact that the Wasserman reaction on the blood of women during the child-bearing period is often of no significance. A mother who has borne one or more children and who is definitely syphilitic frequently has a negative blood Wasserman which will not become positive until she reaches the menopause. In this present case the child gives definite evidence of congenital syphilis and had a positive blood Wasserman on four occasions The mother, on two examinations, is negative to the Wasserman test.

SUMMARY

1—The child has congenital syphilis.

2—Ductus of Botalli is persistent.

3—At the age of six she develops a streptococcus viridans infection with a vegetative endarteritis of the pulmonary artery. There is no accompanying endocarditis.

4—The illness is of a sub-acute ending fatally after a period of six months.

5—There are twenty-three cases on record of patent ductus Botalli associated with a pulmonary endarteritis. Only three in addition to the present report have an endarteritis of the pulmonary artery with no accompanying valvular lesion.

Case No. 2

Hypoplasia of the Aorta

Hypoplasia of the aorta commonly occurs in conjunction with a certain set of cardiac anomalies. These include coarctation of the aorta, anomalies of the aortic arch, bicuspid semilunar valves, persistent left superior vena cava and patent foramen ovale. For this reason the condition of hypoplasia of the aorta is usually classified with congenital cardiac defects. It occurs, however, as an isolated condition, not in association with any cardiac anomaly, and may be manifested by the aorta and its branches being markedly reduced in size, often measuring only ⅓ the normal caliber.

Much discussion has arisen as to whether this isolated condition is a true congenital cardiac anomaly or whether it is purely a post-natal lack of development. Subjects of the thymico-lymphatic constitution possess an aorta which is hypoplastic. Usually this hypoplasia is not pronounced, but occasionally we find the vessel markedly diminished in size, often suggesting a congenital defect. On investigation these cases are found to possess other characteristics common to the thymico-lymphatic constitution, such as, a hyperplastic thymus, generalized lymphoid hyperplasia and hypoplasia of the adrenals. The condition of hypoplasia of the aorta

lunar valves, persistent left superior with no associated cardiac of circulatory defect is probably a manifestation of a definite constitutional type.

Clinical Report

Miss A. A., Aged 17.

Was admitted to the University Hospital 2-13-28, with the chief complaints of dyspnoea, cyanosis, palpitation, and edema. She has always been delicate. At the age of 8 a swelling was first noted in her neck and, at this time, she was not gaining in weight. At the age of 12 a specialist was consulted who prescribed "goitre pills." Shortly after, her symptoms became more marked and the pills were discontinued. When 13 years of age her family doctor found an enlarged heart and a "leaky valve." One year later, 14 years of age, she developed chills and fever. Endocarditis was suspected though the blood culture was negative. In November 1927, aged 16, edema was first noticed. This was accompanied by a slight cyanosis of the lips, fingers, and toes. She was digitalized for the first time in January 1928, one month before admission.

Past History: Had influenza in 1918. No definite history of rheumatic fever, chorea, or scarlet fever. Had her tonsils removed at the age of four.

Family History: Nothing to denote syphilis. No history of heart trouble on either side of the family.

Menstrual History: Began at the age of 14 and were regular until four months ago. Since then have occurred more often and have been more profuse.

Physical Examination: She is intensely dyspneic, very cyanotic, propped up in bed, with a constant anxious expression. There is a marked pulsation of the neck vessels and the thyroid is enlarged.

Lungs: Respirations 32 per minute. There is impaired resonance throughout with dullness at both bases. Many crackling râles are heard at both sides.

Heart: Radial pulse is 104 per minute, weak, but regular. Cardiac dullness extends 12½ cms. to the left and 3 cms. to the right of the mid-sternal line. Sounds are rapid, regular, and weak. A harsh systolic and diastolic murmur is heard at the mitral and aortic areas.

Abdomen: The liver is enlarged and extends two fingerbreadths below the costal margin. There is a slight dullness in both flanks.

Extremities: Show a massive edema most marked in the lower extremities.

Laboratory Findings: Urine—albumin is slightly positive with an occasional hyaline and granular cast. Blood exam.—95% hgb. R.B.C.—7,900,000. W.B.C.—12,300. Differential is not important. N.P.N. of blood 68.2 mgms. Electrocardiogram shows a marked right ventricular preponderance.

Course in Hospital: Death occurred two days after admission. Her temperature was always slightly sub-normal. Orthopnea and cyanosis became very marked. A venesection was done and 500 c.c. of blood withdrawn. This relieved her condition for only a few hours. The patient expired 2/15/28.

Clinical Diagnosis:

1. Aortic insufficiency and stenosis.
2. Mitral insufficiency and stenosis.
3. Congenital heart (type not specified).
4. Polycythemia (secondary).
5. Cardiac failure.

The autopsy was performed two hours after death.

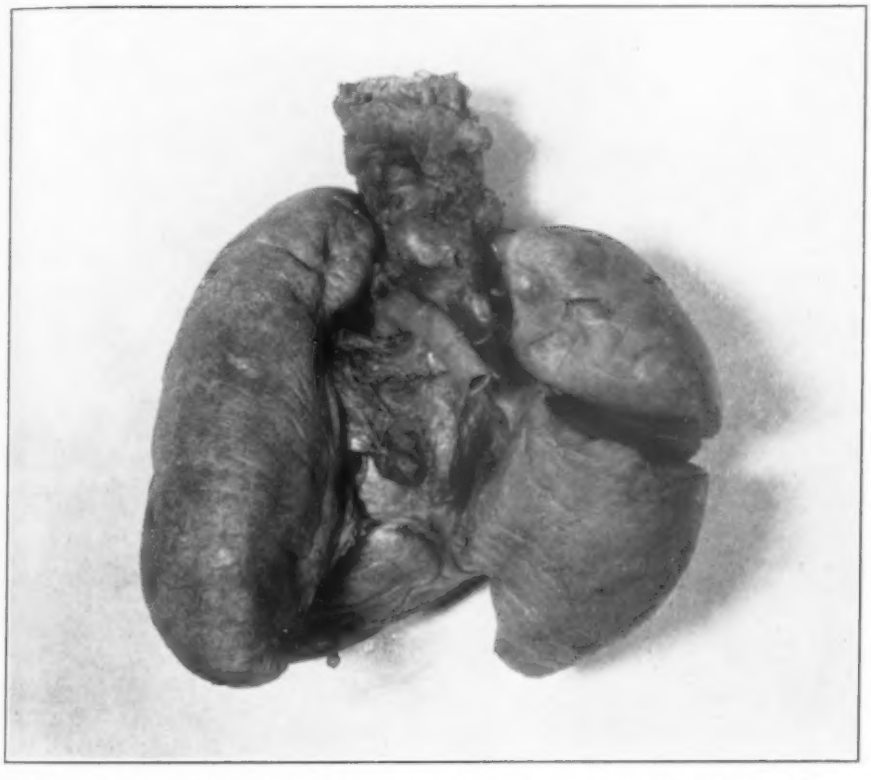
Protocol abbreviated

Miss A. A., aged 17, 2-15-28.

External Examination: Body is that of a young adult female, 159 cms. in length, of a light bony frame. There is a very marked generalized edema. Many small ulcers averaging 5 mm. in diameter are present in the skin of the lower extremities. The face, mucous membranes, and extremities show a marked cyanosis, and there is a dark purple hypostasis present in the dependent portions. There is no clubbing of the fingers or toes.

Abdominal Cavity: Contains 200 c.c. of a slightly turbid, yellow fluid.

Pleural Cavities: Right pleural cavity contains 450 c.c. of a clear, yellow fluid.



No. 4. Posterior view of thoracic organs, showing the marked hypoplasia of the aorta. Case 2.

The left pleural cavity contains 300 c.c. of a similar fluid.

Position of Thoracic Organs: On removing the sternum it is noted that the heart is very markedly enlarged with the pericardial sac lying transversely in the thorax. Both lungs are displaced laterally by the enlarged heart. Measurements of the pericardial sac intact are 18-13-8½ cm.

Anterior Mediastinum: Is entirely filled by the enlarged heart and a hyperplastic thymus.

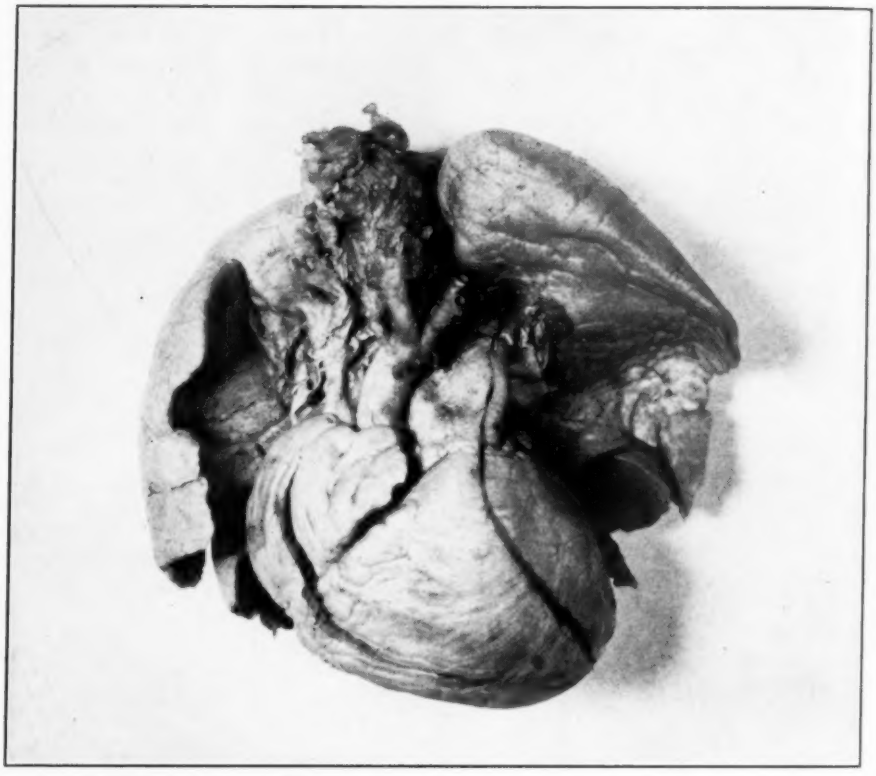
Thymus: Extends downward over the anterior surface of the pericardium. The thymic tissue is markedly congested and definitely hyperplastic.

Pericardium: The wall is not thickened but there is a very definite increase in tension. The sac contains 400 c.c. of a clear fluid. In no place is the pericardium adherent to the heart wall.

Heart: Measures 15 x 11 x 7½ cm., is markedly enlarged. The apex is made up by both ventricles but more so by the right.

Note: The heart, lungs, and aorta are removed intact and placed in 10% formol. Eight days later a careful dissection was done to observe any abnormal anastomosis of the vessels or any congenital defect which may be present.

Left Heart: The left ventricular wall measures 14 mm. The musculature appears slightly hypertrophied. No gross areas of fibrosis are noted. The endocardium in the left ventricular cavity is smooth and shining. There is a marked stenosis of the mitral valve with a generalized thickening of the cusps and occasional areas of calci-



No. 5. Lateral view of thoracic organs, together with the great branches of the arch, as far as the bifurcation. Case 2. The ascending portion of the aorta is shown. The much dilated pulmonary artery is shown

fication. Only the tip of the forceps can be passed through the opening, the diameter measuring 7 mm. In the left auricle the endocardium surrounding the mitral valve is very roughened and deeply congested. The left auricular wall averages 3 mm. in thickness, and there is a very slight dilatation present. The left ventricular cavity is exceptionally small. The aortic valve admits the index finger, but the lumen is diminished in size superior to the valve. There are three cusps present and the coronary vessels arise from the normal locations.

Right Heart: The right ventricular wall averages 17 mm. in thickness, and is markedly hypertrophied. No gross areas of fibrosis are noted. The endocardium is smooth and shining throughout. The tricuspid valve admits three fingers with difficulty, the edges of the cusps are rolled under and appear slightly thickened, but there is no roughening. The right auricle is markedly dilated, with the cavity filled by a large amount of cruor. The auricular wall is hypertrophied, measuring 9 mm. at its thickest portion. The average thickness is 6 mm. The pulmonary valve admits three fingers with difficulty, the cusps appear normal. The foramen ovale is closed.

Pulmonary Vessels: There is a marked enlargement of the pulmonary artery. Superior to the cusps the total diameter is 39 mm. with the diameter of the lumen 34 mm. Throughout the first portion and the main branches the enlargement is constant. The ductus arteriosus is obliterated.

Aorta: This vessel shows a very pronounced hypoplasia throughout its entire

course. Superior to the aortic cusps the diameter is 18 mm. and at the arch measures 13 mm. The size of the vessel remains constant in the descending portion with the diameter at a level of the diaphragm also 13 mm. The vessel wall is decreased in thickness, appearing in proportion to the size of the lumen. Both iliacs arise from their normal position and are also hypoplastic.

All blood vessels are carefully traced and no evidence is found of any anomalous anastomosis. The internal mammary artery is not enlarged on either side, the bronchial, pericardial, and esophageal branches follow their normal course.

Lungs: There is atelectasis of the lower lobe on both sides with a marked congestion and edema of the remaining portions.

Thyroid: Does not appear increased in size. Only a moderate amount of colloid is present.

Adrenals: Are hypoplastic. There is a moderate lipoidosis of the cortex and the medulla appears well preserved.

Female Genitals: The uterus and ovaries appear hypoplastic.

Microscopic Findings

Heart: The left auricle shows marked chronic productive endocarditis with marked fibrosis and areas of active infiltration, mostly mononuclear in type. Mitral valve shows chronic endocarditis with marked fibrosis and calcification with abundant active infiltrations, both polynuclear and mononuclear. Left ventricle shows old sclerosis of endocardium, atrophy of heart muscle with diffuse fatty degenerative infiltration. The right auricle shows marked hypertrophy of wall with fatty degenerative infiltration and very small infiltrations in the myocardium, lymphocytic in character. The right ventricle shows moderate subepicardial fatty infiltration, hypertrophy of the wall with diffuse fatty degenerative infiltration and small lymphocytic infiltrations. There is a slight sclerosis of the endocardium near the tricuspid valve.

Aorta: Markedly hypoplastic. Intima shows early stage of atherosclerosis. No aortitis.

Lungs: Marked brown induration and chronic passive congestion. Bronchioles are dilated. Blood vessels show markedly thickened walls with the lumina very small.

Thyroid: Marked lymphoid hyperplasia. Graves' constitution. Increase of stroma. Colloid fairly abundant. Parathyroid included shows no pathology.

Thymus: Atrophic, but showing abundant thymic remains. Is an atrophic hyperplastic thymus.

Liver: Marked chronic nutmeg liver with beginning central cirrhosis and marked interlobular cirrhosis. Proliferation of small bile ducts in islands.

Adrenals: Very hypoplastic with excessive lipoidosis.

Lymph Nodes: Very marked lymphoid hyperplasia. Hyperplasia of reticulo-endothelium.

Hemolymph nodes: Show marked congestion of the sinuses, and a most marked lipoidosis of the reticulo-endothelium.

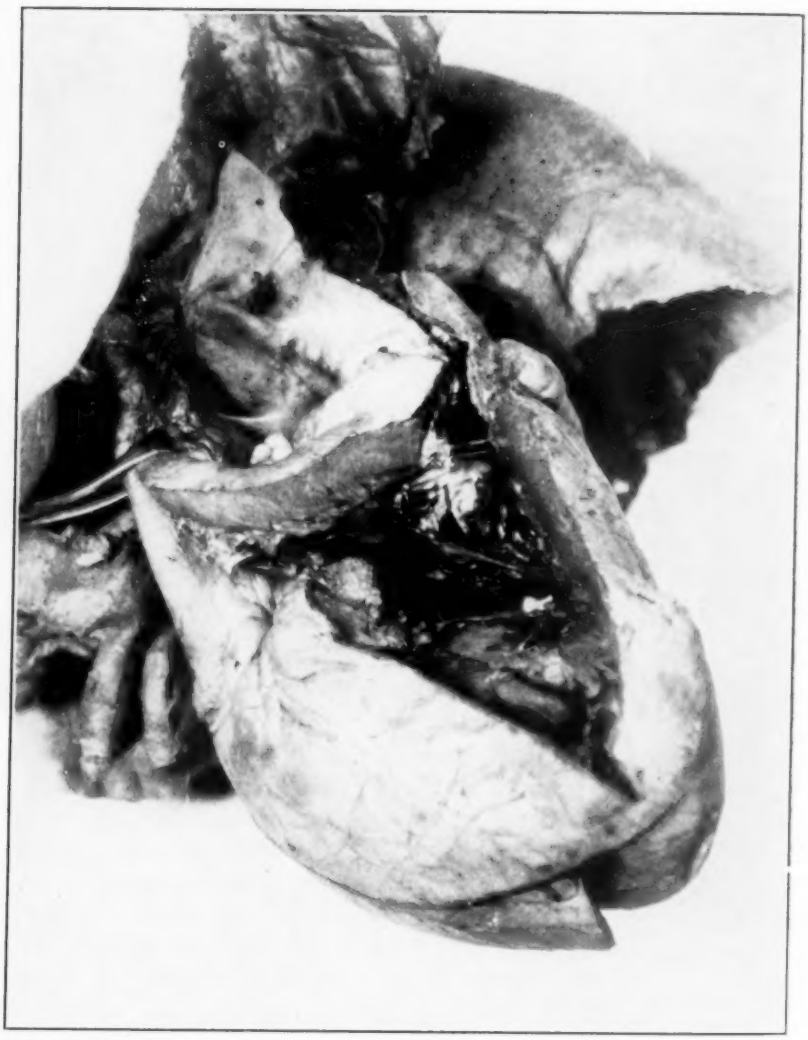
Breasts: Underdeveloped. Small ducts resembling male breasts.

Uterus: Slight subepithelial inflammation. Endometrium is underdeveloped.

Ovaries: Congestion, cystic follicles, and a small number of corpora fibrosa.

Pathological Diagnosis

Old sclerosing chronic mitral endocarditis with button-hole stenosis. Marked hypoplasia of aorta and iliac arteries. Marked dilatation of pulmonary artery. Cardiac hypertrophy with right-sided preponderance. Dilatation of right heart with relative pulmonary insufficiency. Marked brown induration of lungs with areas of atelectasis. Marked nutmeg liver with early central and more marked interlobular cirrhosis. Extreme congestion of all organs. Combined thymico-lymphatic and Graves' constitution, (marked lymphoid hyperplasia of thyroid, atrophic hyperplastic thymus, marked hypoplasia of aorta and



No. 6. Left ventricle opened showing the stenosis of the mitral orifice. Case 2.

adrenals, generalized lymphoid hyperplasia with exhaustion of germ centers). Marked hyperplasia of hemolymph nodes with angiectatic blood sinuses and marked lipoidosis of the reticulo-endothelium. Chromophobe hyperplasia of the pituitary. Hypertrophy of renal glomeruli. Hypertrophy of islands of Langerhans.

Discussion

This subject is definitely of the thymico-lymphatic constitution with some added characteristics of the Graves' type. The marked hypoplasia of the aorta is a manifestation of her constitution, and there are also present many other of the characteristics common to this group. The liver shows a combined cirrhosis; the central cirrhosis is of the Pick's disease type while the interlobular cirrhosis is similar to that found in many of the subjects of the Graves' constitution.

The mitral endocarditis appears to be an old rheumatic infection. Subsequent to the mitral stenosis and sclerosis of the smaller branches of the pulmonary artery, a marked right ventricular preponderance has developed. Cyanosis and polycythemia are manifested in the terminal stages.

This polycythemia is definitely compensatory. Due to the mitral stenosis and marked sclerosis of the smaller pulmonary vessels normal oxygenation of the blood is prevented. Development of the polycythemia is very similar to that in Ayerza's disease where there is a sclerosis of the pulmonary vessels. On both occasions in hospital the blood count showed the red cells over seven million, the highest count being 7,900,000.

Clinically she showed a definite thyroid disturbance which was aggravated by the administration of "goitre pills," probably containing iodine. Microscopic findings prove the thyroid to be of the Graves' constitution type showing the effects of too much iodine.

To summarize:

1—This is a case of marked hypoplasia of the aorta not associated with any cardiac anomaly.

2—She is definitely of the thymico-lymphatic constitution.

3—The mitral stenosis is caused by a chronic endocarditis of the rheumatic type.

4—Due to poor oxygenation of the blood a compensatory polycythemia develops in the terminal stages.

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A Case of Complete Transposition of the Viscera With Electrocardiographic and X-Ray Studies

By Aaron E. Parsonnet, M.D., F.A.C.P., *Attending physician, Beth Israel Hospital, Newark, New Jersey*

TRANSPOSITION of the viscera, although not a rare condition, is interesting. Reports of such cases serve a very useful purpose of putting the physician on guard for these anomalies. To the surgeon, and needless to say, to the patient, a timely diagnosis of visceral transposition is obviously of the greatest importance.

This case came under my observation through the courtesy of Dr. Samuel Roth, of Newark, and holds absolutely true to type as proven by physical findings, electrocardiograms, and X-ray studies.

History: L. F., aged 35, well developed, overnourished white male, was seen by me on May 30, 1928, with chief complaint of "pain over heart." Past history discloses nothing of importance; measles and several attacks of tonsillitis were the only diseases of childhood. He always enjoyed good health and never complained of any symptoms referable to the cardio-vascular or respiratory systems. His father has heart disease at 63, mother living and well at 60.

Physical Examination: The apex beat was not visible and not palpable but best heard in the fifth interspace inside nipple line on the right. All heart sounds were clear, well transmitted through entire precordium, regular, and no murmurs, shocks, or thrills could be elicited. Orthodiagraphic measurements showed the heart to be of normal size, and fluoroscopic examination revealed the dextrocardia clearly; right and left border configurations were normal in outline. Blood pressure readings were systolic 130, and diastolic 85. The lung fields were essentially clear throughout with definite cardiac dulness over right chest. The spleen could not be palpated on the right, but definite liver dullness was present in the left upper quadrant. Under the fluoroscope, typical stomach air bubble seen in right upper abdomen.

The following X-rays were taken on June 6, 1928:—

The electrocardiogram given below shows inversion of the P, QRS, and T waves in the first lead very clearly. All complexes are upright and well formed in second and third leads. These findings are typical of a dextrocardia.

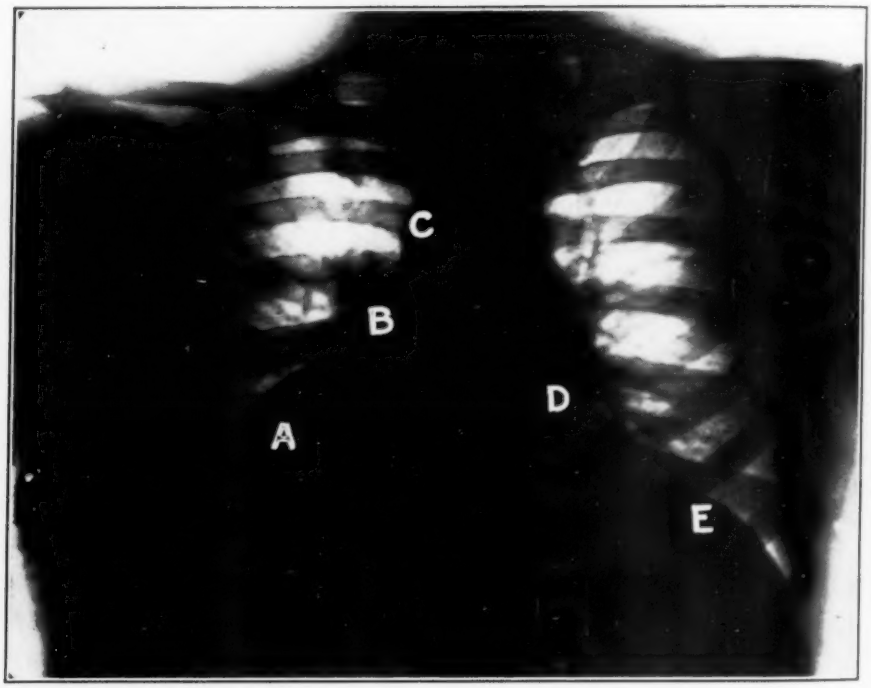

FIG. 1. A. Left ventricle
B. Left auriculo-pulmonic curve
C. Arch of aorta
D. Right heart
E. Diaphragm

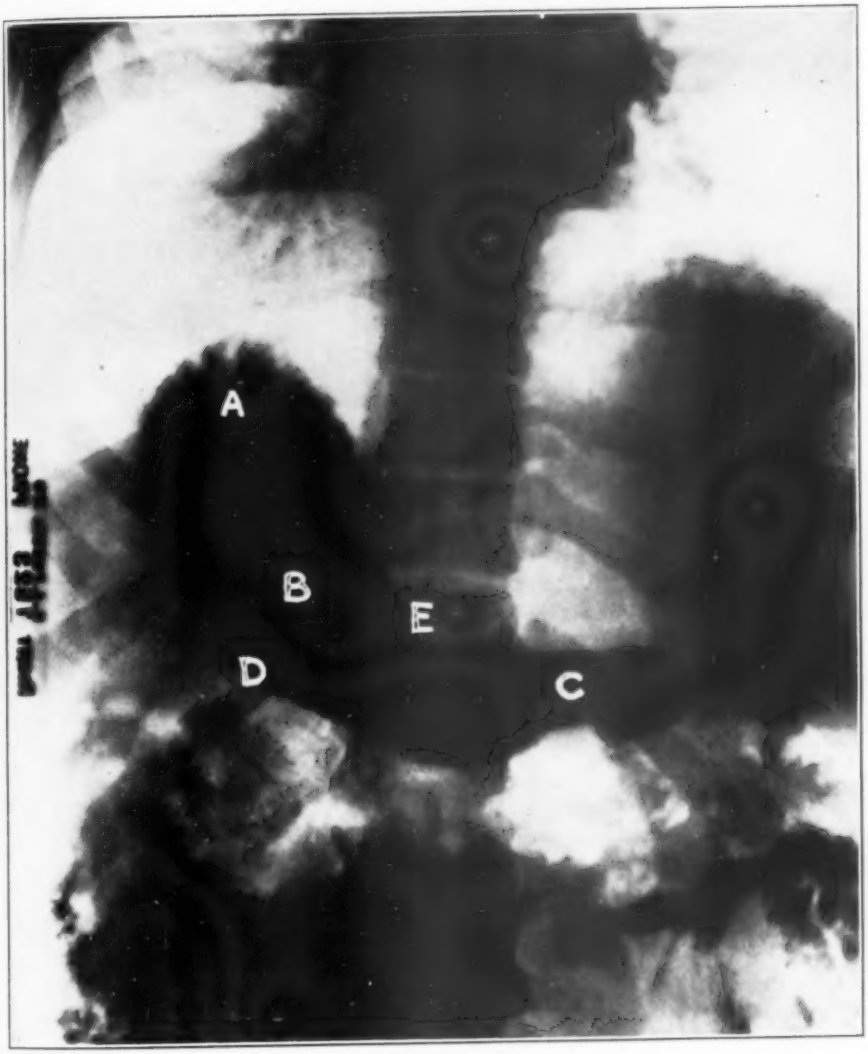

Fig. 2. A. Pars cardia
B. Pars media
C. Pars pylorica
D. Greater curvature
E. Lesser curvature

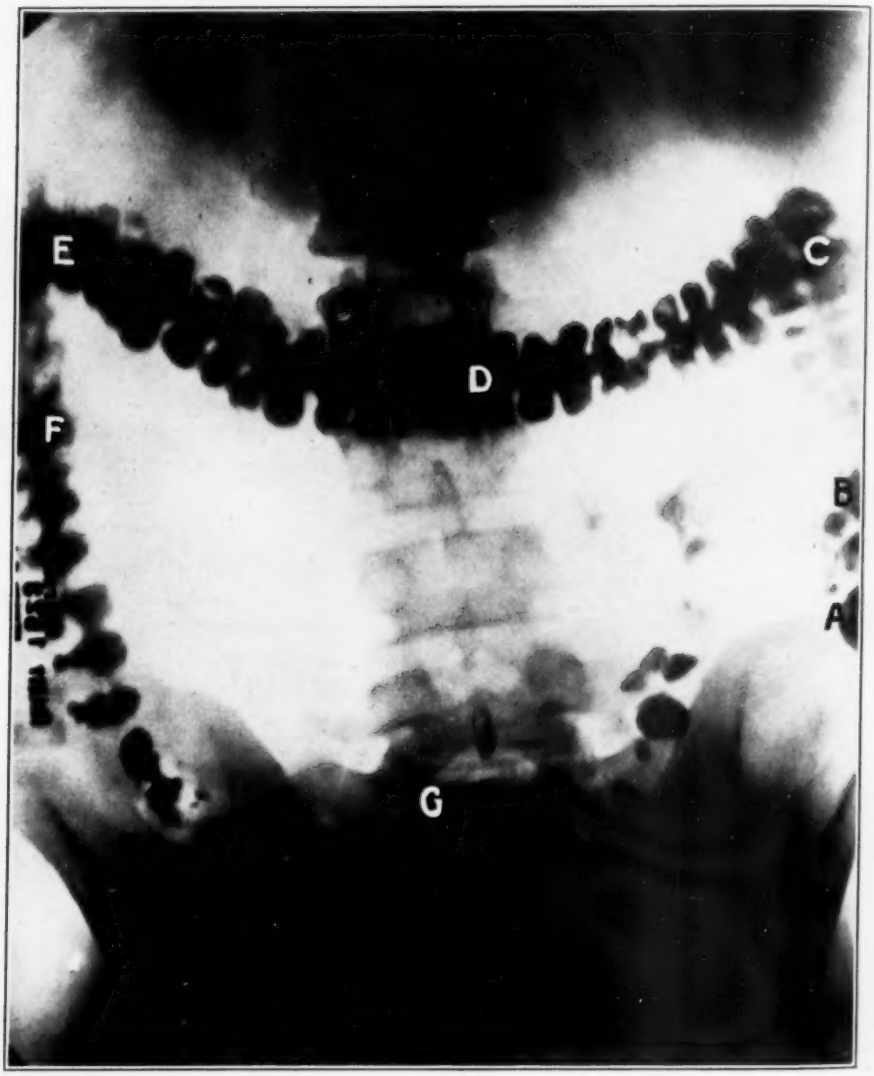

FIG. 3. A. Caecum
B. Ascending colon
C. Hepatic flexture
D. Transverse colon
E. Splenic flexture
F. Descending colon
G. Sigmoid

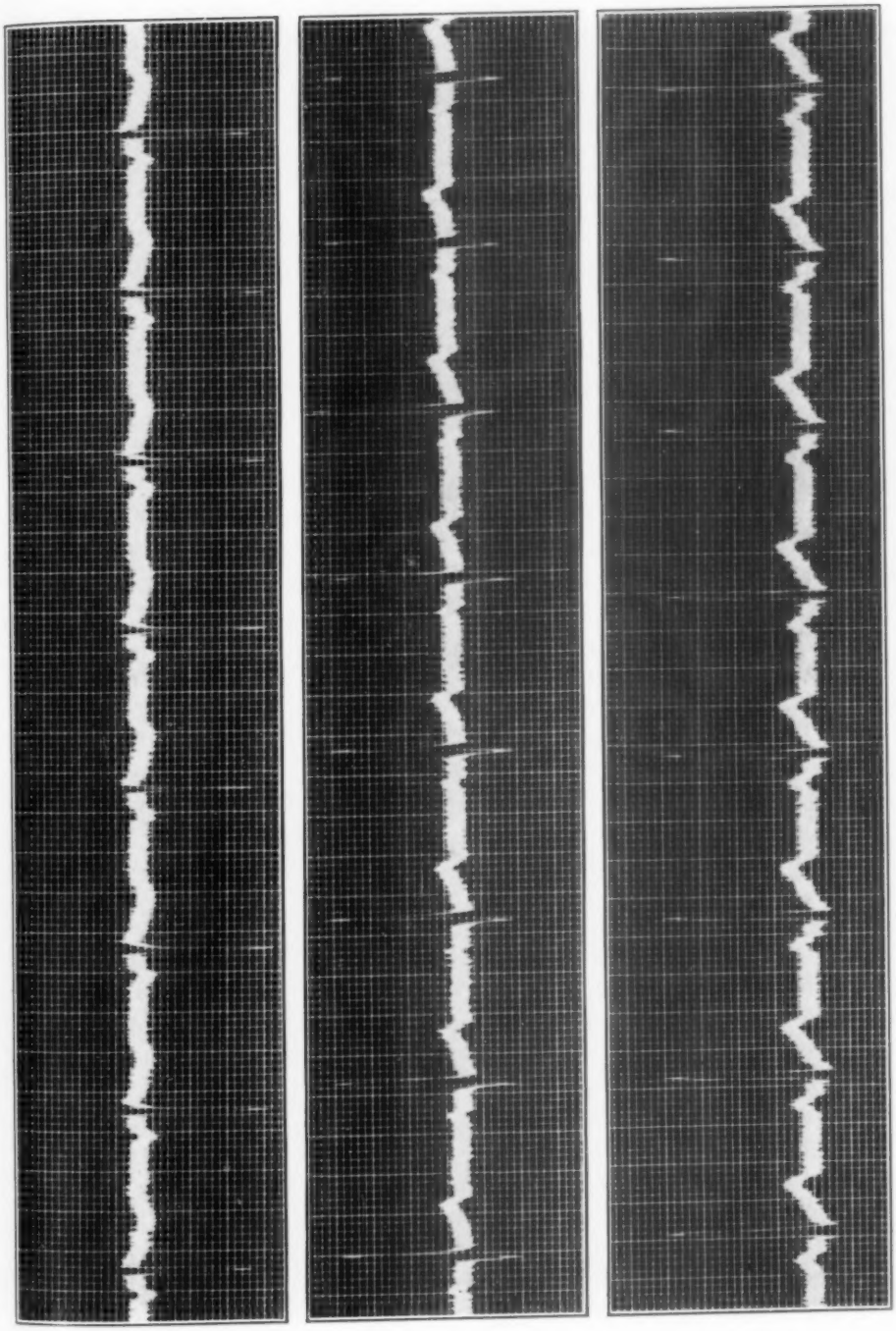

Fig. 4. Electrocardiogram typical of Dextrocardia

Editorial

SYPHILIS AND LIFE INSURANCE

Karl Vajda of Budapest has an article on "Versicherungsmedizinsche Beziehungen der Syphilis" in the number of the Klinische Wochenschrift for January 29, 1929, that deserves careful reading and thoughful attention from every internist who is in any capacity concerned with life insurance examinations. Syphilis has always been one of the most disputed problems of insurance medicine, for two reasons, one, because of the fact that the applicant for insurance, having passed through the active stages of his syphilis, does not mention it to the examiner, and two, because it is extremely difficult, often impossible in most cases to make a diagnosis of latent syphilis in the short time allotted to the medical examination. This diagnosis can be much more easily made under the conditions of private practice. In making the insurance examination the examiner has only a relatively short time for his examination, so he is forced to omit all methods that may be regarded as burdensome to the candidate. Thus the taking of a Wassermann is attended by difficulties, and a spinal reaction is in the majority of cases not even thought of. Although we have made numerous advances in the diagnosis of syphilis since the discovery of the spirochete, yet few of these advances are utilized in life insurance examinations to the advantage of the life insurance companies. Syphilis remains today, as it was thirty years ago, one of the most easily missed conditions in life insurance examinations. There is no criterion of complete healing of the disease. A previous syphilis is and remains a menacing danger to life insurance. The latest statistics show that the mortality of luetics exceeds that of non-luetics by 68 per cent. This means that for every one hundred cases of death within a given age-class for all insured, there are 168 deaths in luetics of the same age-class. The examination of the various disease groups shows that the excess mortality of leuetics over that of malignant neoplasms is 60 per cent, over that of renal diseases 64 per cent, over diseases of the gastrointestinal tract 116 per cent, over suicide 122 per cent, over that of apoplexy 128 per cent, and over that of the group of psychopathic diseases 145 per cent. And this is far from being the whole truth! For in these statistics only those candidates are regarded as luetic who have acknowledged their syphilis to the examiner. How great the number of those who keep silent, and of those who have no knowledge that they possess a latent syphilis! We must assume that the excess mortality of the luetic is very much greater

than indicated by these statistics. We must not forget in this connection that a candidate with manifest syphilis is never accepted for life insurance. Only such luetic individuals who have had syphilis and have passed through a corresponding treatment for the same and show no symptoms, so that they are regarded by the examiner as completely healed are accepted. Herein lies the greatest feature of the syphilis problem. There is at the present time no doubt existing in any one's mind that the *Spirochaeta pallida* is the cause of syphilis, and although many facts relating to the biology of this organism are still unsettled, we do know that it can reproduce in the human body for many decades without producing any symptoms. During this period of latency the patient may enjoy perfectly sound health, and the physician on the most careful examination can find nothing pathologic. Suddenly in the heart, in the aorta, the central nervous system, in the liver, in the kidney the spirochetes begin their deadly work. Involuntarily we must think of that expression of the great clinician Gerhardt, "Die Syphilis schliesst wohl Waffenstillstand, aber niemals Frieden." The great tragedy of it all is that all of these manifestations of this infection are in very many cases diagnosed when all too late for treatment. In the first row stands progressive paralysis as the true horror of life insurance companies. Although the various statistics show that only 2-3 per cent of luetics become paralytic, this percentage would hold only for the insurance companies in case every luetic individual would be insured. It is actually much higher among insured luetics, because mental workers rather than laborers fall victims to paralysis. The percentage of cases of progressive paralysis among the insured luetics is 10-12 per cent. Tabes dorsalis is less important than progressive paralysis from the standpoint of the insurance company, in that this form of syphilis leads to death usually only after several decades. Only a few years ago both of these diseases were regarded as metaluetic or parasyphilitic. Today both are recognized as being nothing else but syphilis of the brain and syphilis of the spinal cord. A similar important rôle is played by syphilis in the etiology of arteriosclerosis, particularly coronary sclerosis, aortic insufficiency, aortic aneurysm, atrophia hepatis flava, aortitis and myocarditis. Further, there is a large group of diseases to which syphilitics are especially predisposed, such as neurasthenia, gout, diabetes mellitus and cancer. Blaschko has made the observation that he has never seen a cancer of the tongue case that did not have a positive Wassermann. Bársony has called attention to the very high percentage of carcinoma of the uterus occurring in luetic women at the Budapest Frauenklinik. The fearful sequelae of syphilis are well shown in the statistics compiled by Pilz and Mattauschek of 4134 officers of the general army who had acquired syphilis between 1880-1900. These officers had been treated 4-5 weeks with an inunction cure, and thereafter dismissed with a potassium iodide prescription. The following year they were again examined and if signs of

syphilis were still present no one troubled himself as to whether the affected officer should have further treatment or not. The mortality statistics of these officers in the next 12 years showed that 132 died of brain syphilis, 193 of progressive paralysis, 113 of tabes dorsalis, 80 of different psychoses, 17 of aortic aneurysm, 101 of organic heart lesions, 44 of apoplexy, 40 of tertiary syphilis, 147 of pulmonary tuberculosis, and 60 committed suicide. While tuberculosis does not belong to the so-called metaluetic diseases, it is an old experience that syphilis predisposes to tuberculosis, and that a mild infection often becomes very malignant fellowing an intercurrent infection with syphilis. In the case of those officers who took only one inunction cure not less than 23 per cent became paralytic, while of those whose treatment extended over two years only 3.23 per cent developed paralysis, while in those who had a four years' treatment there was not a single case. Eleven years ago Blaschko estimated that there were 40 per cent of the male inhabitants and 19 per cent of the female of the city of, Hamburg infected with syphilis, in Berlin 37 per cent male and 17 per cent of the female population. Yet at this time in both of these cities only 3 per cent of the candidates for life insurance acknowledged that they had had the disease. It is easy, therefore, to understand the concern of the life insurance companies in the earlier and more certain diagnosis of latent syphilis. If every luetic candidate for life insurance would acknowledge that he had had the disease, the whole problem becomes reduced to a matter of financial calculation. Given the excessive mortality rate of the luetic in any age class the increase in premium rate can be easily adjusted. But most of the luetics are silent as to their infection. Some actually do not know that they have had the disease, and some have totally forgotten. There remains, therefore, nothing for the examiner but to make the most painstaking examination possible; many Wassermanns should be taken, and if these are repeatedly negative a bacteriologic and serologic examination of the spinal fluid should be made. But it must not be forgotten that a positive Wassermann does not always indicate syphilis, or that a negative Wassermann does not mean the absence of syphilis. The problem, therefore, cannot be settled in a certain number of cases. It is to be remembered also that very often it is the mildest forms of the disease that terminate in progressive paralysis or tabes. Of great importance in the history are the facts of a childless marriage, or repeated abortions on the part of the wife. Also various conditions of the eye are very suspicious. Syphilis plays a much more important rôle in the etiology of iritis and retinitis than is suspected; a parenchymatous keratitis is probably always syphilitic, likewise chorio-retinitis pigmentosa and optic atrophy. Further, of great importance are single neurasthenic disturbances. Since the candidates are always silent as to these subjective symptoms the objective manifestations of the earliest symptoms of progressive paralysis and tabes are of greatest importance. The concentration power of the candidate

should be fully tested; the inability of the incipient case of paralysis to repeat rapidly simple movements of the eyes, tongue and hand should be noted. Here belong also apraxia and dyspraxia, facialis-hypoglossus paresis, tremors of tongue and lips, and above all the pupillary changes. Anisokoria is one of the earliest symptoms occurring many years before the loss of pupillary reflex. The loss of the pupil reflex is in 98 per cent of cases a symptom of tabes or paralysis. In concluding his observations Vajda states that after 4-5 years of scientific treatment insurance may be given a luetic without especial increase of premium. But the number of such candidates is so very small compared to those imperfectly treated that the greatest care must be taken in regard to the latter class. In this group he would give no insurance to any one with active clinical symptoms until perfectly treated. A half year after the end of such treatment in the total absence of symptoms insurance for a period of 15-20 years can be given at normal premium rates. After that period insurance can be continued at a small increase of premium. In case there are no symptoms and the candidate has been well treated without symptoms for the last two years, he may be accepted at normal rates for 15-20 years, if five years has passed since the infection. If ten years have elapsed since the infection then a slight increase of the premium is justified. Because of the action of the International Serum Conference in regard to the evaluation of the negative and positive Wassermann reaction Vajda can no longer support the views of v. d. Berghs that in the case of a negative Wassermann in the candidate for life insurance a small increase of premium should be made, and in the case of a positive reaction a greater increase in the premium rate.

THE MEETING IN BOSTON

From the large number of letters coming in to the Editor's office it would seem that a large attendance is already assured for the Boston Clinical Week. This augurs most promisingly for the success of this meeting. The Boston men have prepared a fine program. Especially attractive is the clinical program which ensures a high grade of clinics suitable for the postgraduate. Attention has been given to the criticisms of the clinics presented at the last two Clinical Weeks to the effect that these clinics were of an order suitable to senior students but not of a postgraduate quality and flavor. The medical visitor to Boston may be assured that all of the clinics presented there are by trained clinicians who have had postgraduate experience, and that the material and the presentation will be worthy of the reputation for high-class postgraduate work which Boston has always enjoyed. In addition to those given by the local men, clinics will be presented by members of the College from other cities, whose reputation for giving postgraduate work of the highest class is well-known. As far as the medical value of the Boston Clinical Week is concerned its success is assured through its program. It behooves the Fellows and

Associates of the College to take advantage of this opportunity for social and intellectual refreshment. As to the other aspects of the meeting in Boston very little can be said in addition to what the special articles on Boston already published in the College News Notes have offered. The historic interest of the city is so great, so interwoven with the history of America, that the visitor to Boston for the first time will have his time wholly filled for him if he does nothing but visit the great historic buildings and scenes which make of the city such a unique object lesson for early American history. The city portion of Boston with its mingling of historic buildings and business blocks has an English atmosphere—the visitor may easily fancy himself to be in London in some of the vistas seen through narrow passage-ways and streets. To the acquainted visitor the art collections of Boston offer much; to the botanist and gardener the Arnold Arboretum is an unfailing joy and interest; to the musician the opportunity for hearing the Orchestra is an enticement; for the educator there is Harvard and the Institute; for the book-lover there is the Widener collection; in fact Boston offers something especially choice in every line of human interest. So then, come to Boston, and plan to take advantage of the many great opportunities, both medical and cultural, that the holding of the Clinical Week in this interesting city makes available to you.

Abstracts

Syphilitic Heart Disease with Failure. By Dudley C. Smith and Raymond D. Kimbrough (The Southern Medical Journal, August, 1928, page 634).

This analysis is based on the study of fifty-six cases admitted to the University of Virginia Hospital between July, 1923 and July, 1927. All of the cases had heart failure and were diagnosed syphilis of the heart or aorta. Syphilis was considered the primary etiological factor; this was proved by autopsy in some of the cases, but in most of them the diagnosis was based on clinical and laboratory data. The cases of heart disease showing what was considered an incidental syphilitic infection and those in which it was thought to be of secondary importance were discarded. In addition to the usual medical investigation consisting of history, physical examination and routine laboratory methods, thirty-four of the patients had electrocardiograms, forty-two were X-rayed and eight were autopsied. Of the fifty-six cases, thirty-nine (69.6 per cent) were negroes, and seventeen (30.4 per cent) were whites. The proportion of negro syphilitic patients to white syphilitic patients in the hospital and out-patient departments was 3 to 2. From these figures it is estimated that syphilitic heart disease occurred one and one-half times as frequently in syphilitic negroes as in syphilitic whites. The average age of the negro patients in this group of admission was 45.8 years as compared with 52.6 years for the white patients. The greater incidence and the earlier occurrence in the negro indicates an increased susceptibility in this race to cardiovascular involvement from syphilis. There were forty-nine male and seven female patients. Fourteen were farmers, twenty were laborers and the occupations of all the others required considerable physical exertion. The average age at admission was 47.7 years. There was a positive history of a genital sore in twenty-five cases. The average interval in these from the initial infection to the onset of failure was twenty-two years. The shortest interval was eight years, the longest forty-one years. Only one case gave a history of early cutaneous lesions. This would seem to confirm the idea expressed by Brown and Pearce in their law of inverse proportion, that severe late visceral involvement occurs more often following mild early reactions. This finding is paralleled by the well substantiated observation that neurosyphilis is relatively less frequent in those patients who have had severe skin symptoms. It is impossible to say whether this is due to different strains of organisms, or to an individual visceral susceptibility. Tabulation of the initial symptoms gave the following results: dyspnea 29 (51 per cent), heart pain 10 (18 per cent), palpitation 10 (18 per cent), substernal pain 3 (5 per cent), weakness 3 (5 per cent), cough 2 (4 per cent), vertigo 2 (4 per cent), headache 1 (2 per cent), and dyspepsia 1 (2 per cent). Some showed more than one initial symptom. Other early symptoms were: edema 28 (50 per cent), dyspnea 14 (25 per cent), heart pain 12 (21 per cent), cough 12 (21 per cent), palpitation 11 (20 per cent), vertigo 10 (18 per cent), weakness 9 (16 per cent), substernal pain 4 (7 per cent), dyspepsia 3 (5 per cent), choking sensation 3 (4 per cent), nervousness 2 (4 per cent), sleep starts 2 (4 per cent), headaches, convulsions, insomnia, cyanosis, hoarseness and "buzzing sound in heart" 1 each. Functionally twenty-five cases presented both congestive and anginal failure, thirty showed congestive failure alone and one anginal failure alone. The abnormal structural findings, based on physical examinations, teleroentgenograms, fluoroscopic examinations, and autopsies were as follows: cardiac hypertrophy 51 (90 per cent), aortic regurgi-

tation 33 (59 per cent), dilated aorta 31 (55 per cent), aneurysm of the aorta 18 (32 per cent), myocarditis 3 (5 per cent), and coronary occlusion 1 (2 per cent). In three of the eight autopsies marked fibrosis and degenerative myocarditis was noted. These were the findings in routine post mortem examinations, and it is probable that microscopical studies would have revealed other instances of specific myocardial changes. Forty-nine of the fifty-six cases had positive blood Wassermann reactions, a percentage of 87.5. Of the remaining seven cases syphilis was evinced by other conclusive findings. Twenty-six of this group had spinal fluid examinations. There were normal findings in fourteen of these tested: in twelve instances, or 46 per cent of those examined, there was positive evidence of central nervous system involvement. The positive spinal fluid findings were the means of confirming syphilis as the etiological factor in some of the cases with negative history and negative blood Wassermann. The average blood pressure in the thirty-three cases of aortic regurgitation was systolic 150, diastolic 60, pulse pressure 81. Case without aortic regurgitation showed systolic 138, diastolic 80 and a pulse pressure of 58. The average blood pressure in all cases was systolic 145, diastolic 74, giving a pulse pressure of 71. The thirty-four electrocardiographic tracings revealed nothing distinctive. Left axis deviation was present in most cases as might be expected in left cardiac hypertrophy. Five patients had partial or complete heart block. The forty-two roentgenographic examinations proved the value of this procedure in determining the structural abnormalities in the heart and aorta. Several cases with negative physical examination showed definite changes such as aneurysm or dilated aorta on examination. This method of examination was also valuable in differential diagnosis from an etiologic standpoint. Forty-eight of the fifty-six cases gave no history of antisyphilitic treatment. The remaining eight gave a history of "internal" treatment, probably mercury and iodids. Most of the cases in which a history of initial infection was obtained began before the modern era of antisyphilitic treatment. The few cases that acquired their infection since the discovery of arsphenamin gave no history of intravenous treatment. Twenty-one of the fifty-six cases are known to be dead, eighteen are known to be alive and the condition of seventeen is unknown. Of the eighteen alive, thirteen are improved and five unimproved. In the group of twenty-one which are dead the average interval from the onset of failure to death was 3.2 years. The average interval since onset of failure in those alive and heard from is 4.1 years. There is undoubtedly a factor in certain of the cases which accounts for a more rapid progression of the heart deficiency, but it has not been determined in this study. In summarizing, these authors find that syphilis is an important etiological factor in heart disease especially in the southern states. The prevention of syphilis will eliminate this group of cardiovascular disorders. The findings in fifty-six cases of syphilitic heart disease with failure are in part presented. The negro race in this country is probably more susceptible to syphilitic heart disease than the white race. Only one in the group of fifty-six cases gave a history of early cutaneous involvement.

Über das Auftreten von temporärem Hyperthyroidismus während der Insulinkur. By F. Högler (Klin. Wochenschr., January 29, 1929).

Högler reports two cases in which the insulin cure was interrupted because of the appearance of a temporary hyperthyroidism, with symptoms of tachycardia, fine tremors, damp skin and maniacal condition of excitement with an increased basal metabolism. After the cessation of the insulin the hyperthyroid symptoms disappeared and the basal metabolism fell to the normal. The production of the basedowian symptoms through insulin points to a correlation between thyroid and islands of Langerhans. Even under normal conditions may any overproduction of insulin produce a certain increased activity on the part of the thyroid. One may suppose that with very labile thyroid function the thyroid will respond to this stimulus in an abnormal manner, thereby inhibiting the increase of assimulation due to in-

sulin. These observations gave rise to the thought that constitutional leanness might have its origin in an abnormal interaction between thyroid and island-apparatus, in that every exogenous or endogenous increase of insulin could lead to an opposing abnormal increased thyreogenic regulation. Observations made upon the action of insulin in cases of the asthenic type did not, however, produce any increase in the basal metabolism or give rise to any basedowian symptoms.

Effect of an Exclusive Meat Diet on Chemical Constituents of the Blood. By CLARENCE W. LIEB and EDWARD TOLSTOI (Proc. of the Soc. f. Exper. Biol. and Med., January, 1929, page 324).

This is a preliminary report of an experiment to study the effect on human beings of an exclusive meat diet of several months duration. The subjects were two Arctic explorers who had spent many years in the Arctic Circle and while there, had lived for the greater part of the time on a practically 100 per cent meat and fat diet. Preliminary to this study they were given careful physical examinations. Both were in excellent condition and shared no evidence of impaired health. Following those examinations studies were made of the respiratory exchange, ketogenesis, protein balance, mineral metabolism, fecal bacteriology, hematology and blood chemistry. This report confines itself to the blood chemical findings. Both men ate nothing but meat, cooked or raw. Two experienced dietitians prepared and served the meat. No subjective untoward efforts were noted. One of the subjects at one time developed nausea and diarrhea while on a lean meat diet; the other suffered from an incidental attack of influenza of 3-4 days duration, with uneventful recovery. Each subject consumed 120-130 gms. of protein and enough fat to total a daily caloric intake of 2200 to 2800. Both men were up and about, and took their exercise in walking. At times when they left the hospital they were accompanied by an attendant so that there might be no criticism as to the supervision of their diet. After 4 months the intensive metabolic studies were temporarily suspended. These subjects reported once a month for blood chemical studies which were continued for a period of 11 months. The communication deals with two questions: 1, Does an exclusive meat diet over a period of 11 months affect the kidneys? 2, What changes, if any, are found in the blood of men receiving such a diet over the period mentioned? The following were studied: N.P.N. urea, uric acid, creatinine, NaCl, sugar, CO_2CP., serum Ca, plasma P, albumin (plasma), globulins, total protein (plasma), A/G, and cholesterol, before the meat diet and after an exclusive meat diet for eight months. All analyses were done in duplicate; whenever there was a question as to the correctness of the procedures analyses were checked at frequent intervals. The data may be summarized as follows: (1) two healthy men, living exclusively on meat diet for the past 11 months, felt no untoward effects, maintained their weight and were in excellent health; (2) no evidence of renal impairment was found; (3) the chemical composition of the blood is little affected, except for a slight increase in uric acid and a temporary lipemia. The latter occurred significantly only after unusual amounts of fat had been taken.

Morbus Basedowii und Perniziöse Anämie. By E. MEULENGRACHT (Klin. Wochenschr., January 1, 1929).

During the last several years Meulengracht has been convinced, through a series of observations, that a certain connection exists between exophthalmic goiter and pernicious anemia, in that a number of cases, exceeding pure coincidence, of pernicious anemia has been seen to develop in individuals that earlier in life had suffered, or were still suffering, from Graves' disease. In the course of the last year he has seen eight cases of pernicious anemia developing in patients with exophthalmic goiter. These patients were all women. It appeared also that in these symptoms of pernicious anemia developed earlier in life than ordinary. The cases of Graves' disease appeared to be of medium severity, and were not distinguished in any way from other cases of the same disease. In some patients the disease developed slowly, and after the manifestation

of the pernicious anemia, either no Graves' symptoms or only mild signs of the disease were present. In some cases a hereditary tendency to pernicious anemia was present in the family; in others no history of a family incidence was obtainable. Two departures in symptoms were noted in the cases; all of these patients were very thin, and in some of the cases marked pigmentation of the skin occurred. Both of these symptoms were referred to the previous Graves' disease. Otherwise the picture presented by the pernicious anemia was the usual one of glossitis, acroparesthesias and achylia. In some of the patients the achylia preceded the anemia by several years; even during the Graves' symptoms. The hematologic picture was the classic one, and the patients reacted characteristically to liver diet. In all of the cases symptoms of Graves' disease preceded those of pernicious anemia, the time period between the two conditions varying from 7 to 28 years. What is the explanation for the occurrence of the two diseases in the same individual? Because of the relative rarity of the two conditions Meulengracht excludes the possibility of the association being purely one of coincidence. The possible action of roentgen treatment is ruled out, since this treatment had been used only in a few of the patients. That the anemia might be the result of a secondary hypothyroidism seems also ruled out by the fact that none of the patients showed any signs of a hypothyroidism, and by the further fact that the basal metabolism in those cases in which it was determined was normal or slightly raised. Further the good results obtained by the liver treatment decided against the diagnosis of myxedema. According to Meulengracht's conception of the cases two possibilities present themselves: 1, that the pernicious anemia developed on the basis of an achylia due to the hyperthyroidism; 2, that an hereditary-biologic connection exists between the two conditions. It is well known that Graves' disease in a large number of cases is accompanied by achylia. Since achylia in general has the pathogenetic significance of pernicious anemia, it might be expected that patients surviving Graves' disease would show a tendency to the development of pernicious anemia. On the other hand both Graves' disease and pernicious anemia show a marked tendency to be hereditary, and certain factors in the genotype must be of significance for the development of both diseases. There lies the possibility that a relationship exists between the hereditary factors concerned, and that the two diseases may, therefore, on this ground show a tendency to occur in the same individuals and in the same families. Meulengracht is convinced that a relationship exists between the two diseases.

Ueber die Aktivierung des Insulins bei Nichtdiabetischen. By E. Vogt (Klin. Wochenschrift, July, 1928, p. 1460).

By activation of insulin one understands a strengthening and a prolongation of its antidiabetic effect through different means. Bertram mixed insulin with albumin bodies, with casaeosan and human serum. The intramuscular injection of the mixture produced in diabetic and in normal rabbits a definite strengthening and prolongation of the lowering of the blood sugar. In further experiments Vogt has produced similar results through the injection of aolan and novoprotin. The most marked effect was produced through the use of the diabetics own serum. Very important is the fact that the activation occurs only in intramuscular injections, but not after intravenous. Bertram regarded the activation as due to a change in the resorption conditions of the insulin. Vogt experimented on non-diabetic women who had recently undergone a fasting cure, adding serum to the insulin. The experiments were carried out at all stages of the sexual cycle. The addition of serum to the insulin gave weakest results when taken at the close of menstruation. From the middle of the intermenstrual period the serum possessed a definite activating power. The high point of activation was reached regularly one or two days before menstruation began. During menstruation the serum showed a lowered activating value. From these investigations carried out on non-diabetic women at the height of their reproductive activity it was found that the activity of insulin could be increased

maximally by the addition of serum taken just before menstruation and possessing the highest content of the female sexual hormone. The addition of the female, albumin-free sex-hormone folliculin influences the action of insulin in a similar way. On the contrary the serum after operative castration or roentgen castration has only a very slight activating power. The irradiation of insulin with the artificial Alpine light or with the roentgen carcinoma dose produces also a definite activation of the insulin. These findings possess a theoretical interest, but possibly also a practical application. It would be a step forward in the insulin therapy of diabetes to be able to use smaller doses of insulin to obtain a given effect, when the high price of insulin preparations is taken into consideration.

Reviews

The Kahn Test. A Practical Guide. By R. L. KAHN, M.S., Sc.D. xii + 204 pages. Bibliography of 236 references. Index. 36 tables, 6 charts, 7 plates. The Wiliams and Wilkins Company, Baltimore, 1928. Cloth, 6 x 9, Price: $4.00.

The purpose of this volume is to present a brief summary of the precipitation phenomenon in syphilis with a detailed discussion of the technical aspects of the Kahn test. Since the publication of the first edition "Serum Diagnosis of Syphilis by Precipitation," considerable data have been accumulated on the fundamental, technical and clinical aspects of the test. This book is practically a second edition of that work. In its preparation it has seemed best to plan to divide the edition into three volumes: one dealing with technique, for laboratory workers; one with the clinical application, for physicians; and one dealing with fundamental aspects, for special students. In conformity with the plan, the present guide may be looked upon as a second edition of the section on "Procedure" in "Serum Diagnosis of Syphilis by Precipitation." An important departure from the first volume is the adherence in the present guide to colloid chemical terminology, although it is not written for colloid chemists. The new terminology is more descriptive. "Antigen suspension" for example, gives a more definite picture than "antigen dilution." Although this guide has been prepared especially for laboratory workers, it is hoped that physicians will in a general way acquaint themselves with its contents, since the intelligent clinical interpretation by physicians of a laboratory method is impossible if they do not possess some general idea of the method; otherwise they are interpreting a name and not a method. The volume gives a detailed discussion of the technique of the Kahn test. One of its aims has been to bring the principles governing precipitation in syphilis into correlation with those governing precipitation in colloidal systems of a non-biologic nature. The first chapter of sixty-four pages is to present the test from a colloid-chemical point of view. These data will appeal to many who are not primarily interested in the diagnosis of syphilis. Chapter Two is concerned with apparatus; Chapter III with reagents; while Chapter IV treats of the standardization of antigen. In Chapter V the Kahn test, its performance, types of reactions, special considerations, interpretation and clinical application are considered. Chapter VI deals with the quantitative procedure with serum, its performance, special considerations and clinical application. In Chapter VII the function of the presumptive procedure, standardization of sensitized antigen, performance of test, special considerations and clinical application are treated. Chapter VIII deals with the procedures with spinal fluid; and Chapter IX, the last one, treats of micro and special procedures. Since the publication of Kahn's first book in 1925 the results obtained by the Kahn Test have been checked and rechecked by laboratory workers in all parts of the world; and it has become the standard routine test in the U. S. Navy, and in many laboratories throughout the world. The advantages of the test are many: it can be made in 45 minutes, in any climate, requires a minimum of apparatus, and scores higher than any other reaction in sensitiveness, in minimum numbers of doubtful reactions and in general dependability in diagnosis. It is invaluable in the diagnosis of early and treated syphilis, and in testing donor's blood in emergency transfusions. It has wholly replaced the Wassermann reaction in many laboratories; and there are at the present time very few laboratories in which the Kahn Test is not employed, either alone or with some other

method. At the Laboratory Conference on the Serodiagnosis of Syphilis, arranged by the League of Nations Health Committee, held in Copenhagen, May 21 to June 4, 1928, 957 sera were examined by Dr. Kahn in comparison with 13 other methods. About half of these sera came from patients suffering from diseases other than syphilis (tuberculosis, gonorrhea, cancer, etc.). The Kahn Test gave no false positive reactions. Experience gained with over 500,000 Kahn tests indicates that this method is highly specific for syphilis. The author is, however, conservative and very wise in his statement that *no laboratory method should be accepted by physicians as the final criterion in the diagnosis of any disease without due regard to clinical manifestations.* A positive (++++, +++, or ++) Kahn reaction should be taken as a very strong indication of syphilitic infection. A very weak (+ or ±) reaction should be taken as a lesser probability. A negative Kahn reaction is an indication of the absence of syphilis. It should be emphasized, however, in spite of the fact that the Kahn test is more sensitive than practically all other serological methods, that a negative reaction does not entirely eliminate the possibility of syphilitic infection. The book is especially to be recommended for its very clear concise style, and conservative presentation.

What Is Life? By AUGUSTA GASKELL. Introduction by KARL T. COMPTON, Professor of Physics, Princeton University; and RAYMOND PEARL, Professor of Biology, The Johns Hopkins University. 324 pages. Index of 1527 references. Charles C. Thomas, Springfield, Illinois—Baltimore, Maryland, 1928. Price in cloth: $3.50 net.

According to this new theory of life, living matter *invariably* consists of an atomic system (a system made up of chemical atoms) that is organized and interpenetrated by another system. The atomic system is matter, or a material system; the intraatomic system is life, not matter, immaterial. The two systems are constituted of the same kind of ultimate units (positive and negative electrons), but are built on different patterns. The structure of living matter *invariably* shows this dual pattern. *Living matter, then, invariably is a dual system, the constitution (or pattern) of which is partly material and partly immaterial; the presence of the immaterial system within the material system constituting the living state.* Since "uniform relations" constitute a "law," the expression of this fact, then, is a statement of *the law of the structure of living matter,* and this law of the structure of living matter defines the difference between *inert* and *living,* and between *living* and *dead* organisms. *Life is a quantity;* it is not matter and is unlike matter. Life consists of *the same constituent units* as does matter; and represents a manner of combination of ultimate units different from the pattern of their combination to form the chemical atoms, or matter. In the living organism, life is an intraatomic quantity. This definition of life applies to *all* life-forms without exception. That which sometimes has been described vaguely as "the life-principle," that which determines the living state (or the state of living), whether of plants or animals, or of man, *alike in all,* is the intraatomic quantity "life." Life forms a definite series, different from the series that from atomic number 1 to atomic number 92, is matter. All life-forms are alike basically in that, or in so far as, life is owing to a peculiar manner of the combination of ultimate units. The differences between one form and another form are determined quantitatively; but there is no *arithmetical progression* (as in the elements), a very large number of different forms and variations of forms being possible. Specific and different properties necessarily characterize the combination of ultimate units after a pattern unlike that of the chemical atoms, or matter; *the peculiar manner of combination that spells life, giving rise to the peculiar properties of life.* Since *all psychic properties attend life,* and life defined as a quantity, it follows that the quantity "life" is identical with "soul." Life and the soul are not, as some have insisted two different problems; nor is the problem of "mind" separate from the problem of life. All problems of the soul and

of the mind are problems of the quantity "life." According to the theory, death of an organism can mean only one thing—the rupture between and the separation of the two systems that constitute the organism. The preceding quotations will sufficiently show the nature of Mrs. Gaskell's argument for the dual nature of the living organism. Her hypothesis is in essential the translation of very primitive conceptions of the body and soul relationship into the language of modern physical chemistry and biology. In truth, one finds nothing more here than the concept of man with a body created out of the dust of the earth into which the breath of life has been breathed, rendered in the scientific jargon of the chemistry, physics and biology of the times. As Compton wisely says in his preface that the honest physicist must admit that he knows no independent experimental evidence to suggest or support the hypothesis of these assumed "Z" combinations of protons and electrons; and he must admit further that he really knows relatively very little about atoms, protons and electrons, and nothing at all about the explanation of life. The decisive proof of Gaskell's theory would involve the proof or disproof of the existence in living matter of combinations of protons and electrons in a different unit structure from the ordinary atoms of the inorganic world. There exists the possibility that her theory can be used as a working hypothesis and that it should be susceptible of experimental proof. Aside from its unproved hypothesis, this book is interesting and stimulating for the concise review of modern physical chemistry and biology given in it. It is a very good example of a hpothesis developed and extended to far-reaching proportions, without a single supporting physico-chemical fact, interesting but unproved. The book is very well printed, and attractive in its format.

The Diabetic Life. Its Control by Diet and Insulin. A Concise Practical Manual for Practitioners and Patients. By R. D. LAWRENCE, M.A., M.D., M.R.C.P. (London), Chemical Pathologist and Lecturer in Chemical Pathology, King's College Hospital. Fourth Edition. 188 pages, 12 illustrations. P. Blakiston's Son & Co., Philadelphia. Price in cloth: $2.50.

Each year since 1925 has seen a new edition of the exceedingly practical little book on the diabetic life. In the one just passed since the last edition there have been advanced no revolutionary ideas on the use of insulin or the treatment of diabetes. More practical details, however, have been incorporated in this volume; and fuller information is offered on the treatment of coma and intercurrent illnesses, since these constitute the most difficult and dangerous problems which the treatment of diabetes presents. Great changes have been made in the tables of food values for carbohydrates, as the result of extensive analyses carried out by the author in association with McCance during the last three years. They discovered that many carbohydrate foods, especially green vegetables, contain much less starch and sugar than formerly supposed. This means that diabetics using their food tables will be allowed larger quantities of some vegetables and fruits than before, and may need in consequence a few more units of insulin a day. It also means that more uniformly accurate dietetic work will be possible, and this is certainly of great importance in experimental work, such as testing new diabetic remedies. This little manual presents the essential facts of the treatment of diabetes in simple concise statements intelligible to both practitioner and layman.

Fistula of the Anus and Rectum. By CHARLES JOHN DRUECK, M.D., F.A.C.S., Professor of Rectal Diseases Post Graduate Hospital and Medical School, Chicago, Illinois. 318 pages, 66 original illustrations. F. A. Davis Company, Philadelphia, 1927. Price in cloth: $3.50 net.

Every practitioner is called upon to treat patients suffering from rectal fistulae, and many times finds himself confronted by a confusing array of symptoms with which he is unable to cope. Little is taught in our medical schools in regard to the subject, and there are numerous and diversified opinions as to both etiology and treatment. In the presentation of this monograph the author his put together the ana-

tomical, pathological, physiological and clinical knowledge gained through years of study of a large number of cases that had been required to submit to more than one surgical operation, and, even then, went on uncomfortably through life. In the treatment of rectal fistulae the physician must remember that the technical procedures incident to the removal of the fistula are only the first steps in the treatment, and that he must always preserve the functions of the rectum and anus. In a region the anatomy of which is so complicated and intricate as the perineum, the preservation of function becomes a complicated problem. Any one may introduce a director through a fistula into the rectum and rip up the overlying structures, but the carefully planned procedure which preserves vital tissues, even though the sinus goes through or around them, reflects credit on the surgeon. No matter how complicated the fistula, the functions of the sphincters, levator ani, and the important nerve and blood vessel trunks must be preserved. The technical methods used in bringing about successful results in the treatment of rectal fistulae are given in careful detail in this book. It represents a very thorough and careful presentation of the subject.

Diseases of the Blood. By A. PINEY, M.D., M.R.C.P., Research Pathologist, Cancer Hospital, London. 195 pages, 20 illustrations, six in color. P. Blakiston's Sons & Company, Philadelphia, 1928. Price in cloth, $4.00.

The author thinks that, while it may seem that little excuse exists for the publication of yet another book on the blood, there is no other book that covers quite the same ground as the present one. The student does not, as a rule, want much hematologic detail, and the practitioner only requires bare outlines of immediate practical value. The present book is an attempt to supply such information. It is hoped that it will also serve as an introduction to more detailed treatises which often fail in their intention by presuming that the reader is already acquainted with the more elementary aspects of hematology. In spite of the predominantly practical nature of this book, it has been thought necessary to devote rather more space than is usual to a consideration of the underlying anatomical changes in the hemapoietic organs, because without some knowledge of these, it is impossible to obtain the maximum of information from the blood picture. Following an introduction, the various chapters treat in succession of leukocytic variations, erythrocytic variations, leukemia, diseases allied to the leukoses, myelomas, some forms of anemia, anemias of childhood, hemorrhagic diathesis, polycythemia, forms of splenomegaly and symptomatic blood changes. Following these there is an appendix treating of hematologic technique, blood groups and blood transfusion, and X-rays and radio-active substances. A useful glossary completes the book. This little book is as much up to date as any text book can be, particularly in reference to the pathologic anatomy underlying the hematologic changes. It is by far the most practical work on hematology that the reviewer knows of; it is highly to be recommended to the medical student and the practitioner. The latter will find in it an excellent resumé of the clinical symptoms, as well as of the known pathology of each of the known hematologic conditions, with a sufficient consideration of their treatment.

Clinical Physiology. (A Symptom Analysis) In Relation to Modern Diagnosis and Treatment. A Text for Practitioners and Senior Students of Medicine. By ROBERT JOHN STEWART MCDOWALL, D. Sc., M.B., F.R.C.P. (Edin.), Professor of Physiology, King's College, University of London. With an Introduction by W. D. HALLIBURTON, LL.D., F.R.C.P., F.R.S., Emeritus Professor of Physiology, King's College, University of London. 383 pages, four plates. D. Appleton and Company, New York, 1927. Price in cloth: $3.50.

This volume is an attempt to present some of the facts of Physiology and their applications in General Medicine in a form which fits in conveniently with pathological and clinical teaching. This aim has made necessary a complete departure from the usual arrangement of physiological text

book, and it will be realized that it is not easy to collect material over such a wide and varied field and yet to keep the volume within easily readable limits. The book is intended primarily for senior students and practitioners of medicine who are too busy to read more exhaustive monographs, but who are nevertheless anxious to familiarize themselves with the physiological principles upon which so many of our modern methods of diagnosis and treatment are based. The author's experience as a teacher of clinical medicine gave him an opportunity to study in some detail how far the average medical student was able to adapt his knowledge of the science of physiology to his practical requirements. While it was fully realized that the study of Physiology in its more scientific aspect was in every way desirable, it was clearly seen that for the adequate appreciation of the signs and symptoms of disease more was necessary than is usually taught by the physiologist or clinician. For example, it is extremely difficult, indeed almost impossible from the study of ordinary text book physiology, for the student to see why a cardinal sign of cardiac disease should be breathlessness. This is a textbook then of applied or bedside physiology, and is of great value as a practical correlating branch of study, especially for medical seniors and internes. It achieves its object very successfully, and is to be recommended for senior reading.

A Manual of Materia Medica. For Medical Students. By E. Quin Thornton, M.D., Assistant Professor of Materia Medica in the Jefferson Medical College. Second Edition, Thoroughly Revised. 384 pages. Lea and Febiger, Philadelphia, 1927. Price in cloth: $4.00.

The tenth decennial revision of the United States Pharmacopoeia became effective on January 1, 1928. Among many other changes in that book, there were 40 pharmacopoeial articles added, 191 deleted and 47 official titles changed. On account of these extensive changes it became necessary to revise this manual, and the author has taken advantage of this opportunity to condense, rearrange and practically rewrite it. An object constantly kept in view has been to arrange and condense the text so that all articles of the United States Pharmacopoeia might be lectured upon by the teacher, and studied by the student within the hours devoted to the subject of materia medica during the college year. The book is divided into three parts. In Part I a limited number of pages are devoted to Posology, Methods of Administering Drugs, Common Incompatibilities, Weights and Measures and the Latin Language as applied to Prescription Writing; Part II discusses Inorganic Articles of the Pharmacopoeia arranged in closely allied groups; Part III includes all Organic Official Substances arranged according to their most common uses. The author assumes that it is of little value for medical students to know the botanical origins or the minute structure of roots, leaves, etc., or know the method of manufacturing chemicals; but he believes it of prime importance for them to know Latin and English names and synonyms, the general appearances and characters of drugs and remedies, important constituents, percentage strengths of heroic remedies, composition of the compound galenical preparations, common incompatibilities, methods of administering and doses of all pharmacopoeial drugs. This volume is an eminently practical exposition of the ground covered by it; it represents a concise and careful condensation of materia medica knowledge, freed from unnecessary extraneous material.

René Theophile Hyacinthe Laënnec. A Memoir. By Gerald B. Webb, M.D., President, Colorado School of Tuberculosis, Colorado Springs; U. S. Government Delegate to the Laënnec Centenary, Paris, December, 1926. 146 pages, 13 full-page plates. Paul B. Hoeber, Inc., New York, 1929. Price in cloth: $2.00. Special Edition of 120 copies on Kelmscott Hand-made paper, with illustrations on Japanese Vellum, signed by the author, $12.50.

Heretofore there has been no attempt to give a complete picture in the English language of the immortal French physician, Laënnec, and to few outside of the medical

profession is his name known. The present volume is the result of an address given by Webb before the Denver Clinical and Pathological Society on February 9, 1926, in commemoration of the centenary of the death of Laënnec. Rewritten and elaborated for publication that address appears in the form of the present volume. In it Webb sketches in a thoroughly delightful manner the story of Laënnec's birth and family, his boyhood and school life, the period of his medical study at Nantes and in Paris, the entrance into practice and teaching, and his discovery of the stethoscope. In August, 1819, there appeared his monumental work "Del 'Auscultation Médiate, on Traité du Diagnostic des Maladies des Poumons et du Coeur, fondé principaletment sur ce nouveau moyen d'Exploration," which met the usual harsh reception given to works of genius on first appearance, especially in his own country, although well received elsewhere. The story continues with descriptions of his illness, return to Paris and the rather pathetic events of his last days. Throughout this interesting biography the author reveals his intensive admiration for, and deep sympathy with his subject, whose name remains one of the greatest in the history of tuberculosis. It is a well-told biography; the essential facts are all there, with a sufficient background of atmosphere. The interesting illustrations are for the most part taken from the volumes on Laënnec published in 1912 and 1920 by Alfred Rouxeau. This volume is another one of Hoeber's little achievements in the field of medical history which should be in the possession of every man interested in the medical life.

College News Notes

PROGRAM

THIRTEENTH ANNUAL CLINICAL SESSION

BOSTON COMMITTEES

JAMES H. MEANS, *General Chairman*

COMMITTEE ON ARRANGEMENTS

JAMES H. MEANS
WILLIAM B. BREED
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PRELIMINARY PROGRAM
ANNUAL CLINICAL SESSION
THE AMERICAN COLLEGE OF PHYSICIANS
APRIL 8-12, 1929

Monday, April 8, 1929

OPENING SESSION, 2:30 O'CLOCK

Hotel Statler Ballroom

1. Addresses of Welcome. David L. Edsall, Dean of Harvard Medical School. Alexander S. Begg, Dean of Boston University Medical School. A. Warren Stearns, Dean of Tufts College Medical School. John M. Birnie, President of Massachusetts Medical Society. Lincoln Davis, President of Suffolk District Medical Society.

2. Reply to Addresses of Welcome. Charles F. Martin, President of The American College of Physicians.

3. Tuberculosis: A Confession of Faith. Lawrason Brown, Saranac Lake, N. Y.

4. (Title not yet announced.) Lewellys F. Barker, Baltimore.

5. Juvenile Diabetes. I. M. Rabinowitch, Montreal.

6. Glycosuria. James E. Paullin, Atlanta.

7. Clinical Aspects of Paroxysmal Hypertension. M. C. Pincoffs, Baltimore.

EVENING SESSION, 8:00 O'CLOCK
Hotel Statler Ballroom

Symposium on Deficiency Diseases

1. The Fundamental Nature of Deficiencies. George R. Minot, Boston.

2. Pathology of Deficiencies. S. Burt Wolbach, Boston.

3. Biochemistry and Physiology of Deficiencies. George R. Cowgill, New Haven.

4. Pernicious Anemia. Randolph West, New York.

Tuesday, April 9, 1929
MORNING, 9:00 TO 12:00 O'CLOCK
Hospital Clinics

AFTERNOON, 2:30 TO 5:00 O'CLOCK
Hotel Statler Ballroom

1. Fatigue and Infection. W. L. Holman, Toronto.

2. Neoplasms. J. B. Murphy, New York.

3. Specific Dynamic Action of Protein, Fat and Carbohydrate in Altered States of Nutrition. Edward H. Mason, Montreal.

4. The Relation of Neisserian Infection to the Various Types of Arthritis. O. H. Perry Pepper, Philadelphia.

5. The Fallacy of Vaccine Therapy. Charles C. Bass, New Orleans.

6. The Treatment of Angina Pectoris. Harlow Brooks, New York.

7. The Coronary Problem. Arthur R. Elliott, Chicago.

8. Clinical Aspects of Trichiniasis. Lewis A. Conner, New York.

9. An Intensive Clinical Study of a Graphic Method of Recording Blood Pressure. Louis F. Bishop and Louis F. Bishop, Jr., New York.

EVENING SESSION, 8:00 O'CLOCK
Hotel Statler Ballroom

1. Psychiatry in Relation to Medicine. Austin F. Riggs, Stockbridge, Mass.

2. Syphilis of the Adrenals and Its Relationship to the So-called Idiopathic Addison's Disease. Aldred S. Warthin, Ann Arbor.

3. Lung Syphilis. R. I. Rizer, Minneapolis.

A *smoker* will follow this session.

Wednesday, April 10, 1929
MORNING, 9:00 TO 12:00 O'CLOCK
Hospital Clinics

AFTERNOON, 2:30 O'CLOCK
Hotel Statler Ballroom

1. The Treatment of General Paresis. Harry C. Solomon, Boston.

2. Psychiatry's Part in Preventive Medicine. Arthur H. Ruggles, Providence.

3. The Need of Emotional Data in the Medical History. John Favill, Chicago.

4. Milder Forms of Coronary Obstruction. James B. Herrick, Chicago.

5. The Failing Heart of Middle Life. David Riesman, Philadelphia.

6. Hypertension. George C. Hale, London, Ont.

7. Undulant Fever in the United States. George Blumer, New Haven.

8. (Title not yet announced.) Robert A. Cooke, New York.

9. Tobacco Smoking and Gastric Symptoms. Irving Gray, Brooklyn.

EVENING SESSION, 8:00 O'CLOCK
Hotel Statler Ballroom

1. Serums and Vaccines in the Prevention and Treatment of Disease. Benjamin White, Boston.

2. Clinico-Roentgenological Conference. M. C. Sosman and Associates, Boston.

Thursday, April 11, 1929
MORNING, 9:00 TO 12:00 O'CLOCK
Hospital Clinics

AFTERNOON, 2:30 O'CLOCK
Hotel Statler Ballroom

1. The Treatment of Acute Asphyxia. Cecil K. Drinker, Boston.

2. The Significance of Abnormal Metabolic Features in the Management of Thyrotoxicosis. Walter W. Palmer, New York.

3. Can or Will the Internist Practice Preventive Medicine? George H. Bigelow, Boston.

4. Factors in the Prognosis of High Blood Pressure. W. W. Herrick, New York.

5. The Carotid Sinus Reflex (Hering); Its Use in the Diagnosis and Treatment of Certain Cardiovascular Diseases. C. Saul Danzer, Brooklyn.

6. Lead Poisoning from Snuff. Raymond J. Reitzel, Galveston.

The General Business Meeting of The College will be held at 4:00 in the Hotel Statler Ballroom. All Masters and Fellows should attend.

EVENING, 7:00 O'CLOCK

Annual Banquet of The College
To be followed by a Dance.

Address: George E. Vincent, President of Rockefeller Foundation.

Friday, April 12, 1929
MORNING, 9:00 TO 12:00 O'CLOCK
Hospital Clinics

AFTERNOON, 2:30 O'CLOCK
Hotel Statler Ballroom

1. Motion Picture: Demonstrating Its Value in Teaching Electrocardiographic Interpretations of Cardiac Arrythmias. Joseph B. Wolffe, Philadelphia.

2. Dr. William Dunlop and Pioneer Canadian Medicine. J. W. Crane, London, Ont.

3. Rheumatic Fever. Homer F. Swift, New York.

4. (Title not yet announced.) J. C. Meakins, Montreal.

5. Results to Be Expected in Malignant Disease Treated by Radiotherapy. George E. Pfahler, Philadelphia.

6. The Problem of the Nervous Patient. Charles H. Nielson, St. Louis.

7. Endogenous Obesity—A Misconception. L. H. Newburgh and M. W. Johnston, Ann Arbor.

EVENING SESSION, 8:00 O'CLOCK
Hotel Statler Ballroom
Convocation Exercises

The General Profession is cordially invited. No special admission tickets are required.

1. Convocation Ceremony.

2. President's Address. Charles F. Martin, Montreal.

PRELIMINARY PROGRAM OF SPECIAL CLINICS AND DEMONSTRATIONS

This year the general session will be held in the afternoons and evenings, while clinics and demonstrations will be held in the mornings from 9:00 to 12:00.

Special Admission Cards required. Clinic reservation forms and full directions will accompany the Final Program. Reservations may be made by mail or daily at the Registration Bureau.

Special clinics and demonstrations will be held as follows:

A

BETH ISRAEL HOSPITAL

Program in charge of Herrman L. Blumgart

B

BOSTON CITY HOSPITAL

1. (A guest will give a clinic at this time; the name will be announced later.)

2. The Progress of the Boston City Hospital. John J. Dowling, Superintendent.

3. Treatment of Pneumonia. Demonstration of Cases. Edwin A. Locke.

4. Clinic of Unusual Cases. Francis W. Palfrey.

5. Pernicious Anemia. Demonstration of Cases. William B. Castle.

6. Treatment of Anemias. Demonstration of Cases. George R. Minot.

Wednesday, April 10, 1929

1. (A guest will give a clinic at this time; the name will be announced later.)

2. Gastro-Intestinal Cases. Franklin W. White.

3. Cardiac Cases. William H. Robey.

4. Nephritis Cases. William R. Ohler.

5. The Surgical Treatment of Pulmonary Tuberculosis. Demonstration of Cases. Edward D. Churchill.

Hypertension and Arteriosclerosis. Demonstration of Cases. Soma Weiss.

Thursday, April 11, 1929

1. Cardiac Cases. Edward N. Libby and Thomas J. O'Brien.

2. A Case Illustrating the Value of the Electrocardiogram. James M. Faulkner.

3. Epilepsy. William G. Lennox.

4. Diseases of the Coronary Vessels. Demonstration of Cases. Joseph T. Wearn.

5. Peptic Ulcer. Demonstration of Cases. Maurice Fremont-Smith.

6. Neurological Cases. Stanley Cobb.

7. (A guest will give a clinic at this time; the name will be announced later.)

Friday, April 12, 1929

1. (A guest will give a clinic at this time; the name will be announced later.)

2. Cases of Disease of the Hemopoietic System. Ralph C. Larrabee.

3. Lymphoblastoma. Demonstration of Cases. Henry Jackson, Jr.

4. Tropical Diseases. Demonstration of Cases. George C. Shattuck.

5. Fluoroscopic Diagnosis in Chest Conditions. Demonstration of Cases. Harold W. Dana.

6. Carcinoma of the Head of the Pancreas. Demonstration of Cases. Irving J. Walker.

C

BOSTON CITY HOSPITAL
THORNDIKE MEMORIAL LABORATORY

Wednesday and Thursday
April 10 and 11
Between 10:30 and 12:30

Demonstration of Researches Concerning the Following Topics

Dr. Castle and Associates..... Anemia
Dr. Jackson and Associates..... Malignant Tumors
Dr. Lawrence and Associates..... The Physiology and Pathology of White Cells
Dr. Lennox ..... Epilepsy
Dr. Minot and Associates..... The Blood
Dr. Nye and Associates..... Bacteriological Problems
Dr. Wearn and Associates..... The Capillaries
Dr. Weiss and Associates..... Vascular Problems

BOSTON CITY HOSPITAL
SOUTH DEPARTMENT

Program in charge of Edwin H. Place

Ward visits on (1) diphtheria, (2) scarlet fever, (3) a few of the other minor groups such as chicken pox, mumps, measles and whooping cough.

Amphitheater demonstration of cases of chronic laryngeal injury and other damages resulting from contagious diseases.

E

BOSTON DISPENSARY

TUESDAY, APRIL 9, 1929

1. Heart Disease. David Davis.
2. Essential Hypertonia. David Ayman.
3. Neurological Clinic. A. Warren Stearns.
4. Obesity. Mark Falcon-Lesses.
5. Gastro-Intestinal Clinic. Percy B. Davidson.

WEDNESDAY, APRIL 10, 1929

1. Bronchiectasis. William Dameshek.
2. Psychalgia. Joseph H. Pratt.
3. Arthritis. John D. Adams.
4. Chronic Pancreatic Disease. Bert B. Hershenson.
5. Tuberculosis. H. Louis Kramer.

THURSDAY, APRIL 11, 1929

1. Neurosyphilis. Arthur Beck.
2. Neurasthenia. Joseph H. Kaplan.
3. Nephrosis. Tobert W. Buck.
4. Domiciliary Medicine in Clinical Teaching—Selected Case. Osadore Olef.
5. Domiciliary Medicine in Clinical Teaching—Selected Case. Charles Korb.
6. Diabetes. James H. Townsend.

F

CHILDREN'S HOSPITAL

Program in charge of Kenneth D. Blackfan

G

HOMEOPATHIC HOSPITAL
EVANS MEMORIAL CLINIC

TUESDAY, APRIL 9, 1929

1. Sterility Clinic. Special Emphasis to be Placed on the Constitutional Factors in Sterility. S. R. Meaker and A. W. Rowe.

WEDNESDAY, APRIL 10, 1929

Endocrine Clinic

1. Endocrine Diagnosis and Therapy. Charles H. Lawrence.
2. Endocrine Disorders Associated with Otosclerosis and the Menière Syndrome. D. W. Drury.
3. Eye Findings in Endocrine Disorders. W. D. Rowland.
4. Cases Presenting Outward Evidence of Endocrine Disorders Found on Study not to have Endocrine Disturbance. A. W. Rowe.
5. Dementia Praecox. L. G. Hoskins.
6. The Follicular Hormone. J. C. Janney.
7. Discussion on Sugar Metabolism as Influenced by Insulin in Pituitary Disease. H. Ulrich and A. W. Rowe.

THURSDAY, APRIL 11, 1929

General Medical Clinic

1. Heart Clinic. W. D. Reid.
2. Intestinal Migraine. C. W. McClure.
3. Neurology. N. H. Garrick.
4. Lung Abscess, Diagnosis and Treatment: Bronchoscopy, the Use of the Bronchoscope in Diagnosis and Treatment. L. R. Johnson.

FRIDAY, APRIL 12, 1929

(Program to be announced later.)

H

MASSACHUSETTS GENERAL HOSPITAL

1. Clinic by James E. Paullin, Atlanta.
2. Thoracic Clinic. Frederick T. Lord.
3. Cases of Hypertension. William B. Breed.
4. Cardiac Clinic. Howard B. Sprague.
5. Endocrine Clinic. Walter Bauer and Dwight L. Sisco.

WEDNESDAY, APRIL 10, 1929

1. Clinic by Lewellys F. Barker, Baltimore.
2. Demonstration of Medical Cases. William B. Robbins.
3. Pediatric Clinic. Fritz B. Talbot and Harold L. Higgins.
4. Clinico-pathological conference. Richard C. Cabot and Tracy B. Mallory.
5. Diabetic Clinic. Roy R. Wheeler.

THURSDAY, APRIL 11, 1929

1. Clinic by O. H. Perry Pepper, Philadelphia.
2. Neurological Clinic. James B. Ayer.
3. Psychotherapy of Gastro-Intestinal Diseases. William Herman.
4. Gastro-Intestinal Clinic. Chester M. Jones.
5. Indications for Splenectomy. Arlie V. Bock.
6. Cases of Pernicious Anemia. Wyman Richardson.

FRIDAY, APRIL 12, 1929

1. Clinic by J. C. Meakins, Montreal.
2. Demonstration of Cases. Gerald Blake.
3. Medical Clinic. James H. Means.
4. Demonstration of Cases. F. Dennette Adams.
5. Anaphylaxis Clinic. Francis M. Rackemann.

I

NEW ENGLAND BAPTIST HOSPITAL

Program in charge of Albert A. Hornor

J

NEW ENGLAND DEACONESS HOSPITAL

Program in charge of Elliott P. Joslin

1. Carcinoma of the Colon and Colitis from the Surgical Point of View. Daniel F. Jones.
2. Gastro-Intestinal Cases. Sara M. Jordan and Chester Kiefer.
3. Thyroid Cases. Frank H. Lahey.
4. Pedigreed Diabetics. Elliott P. Joslin.
5. Surgery in Diabetics. L. S. McKittrick.
6. The Pathology of Diabetes. Shields Warren.

There will be further additions to this program including clinics by larynologists, ophthalmologists, gynecologists and roentgenologists.

K

PETER BENT BRIGHAM HOSPITAL

1. Diagnosis of Certain Forms of Heart Disease. Lewis A. Conner, New York.
2. Chronic Myocardial Disease. Henry A. Christian.
3. Results of Treatment of Duodenal Ulcer. E. S. Emery.
4. Some Considerations on the Relation of Cardio-Renal System to Surgery of the Urinary Organs. William S. Quinby.
5. Bronchoscopy in Lung Disease. Lyman C. Richards.

WEDNESDAY, APRIL 10, 1929

1. Cardiac Disease, the Result of Infectious Processes. James B. Herrick, Chicago.

2. Gallbladder Disease. Channing Frothingham.

3. Bronchial Asthma. I. Chandler Walker.

4. Anemia. William P. Murphy.

5. Thrombophlebitis. John Homans.

THURSDAY, APRIL 11, 1929

1. Mitral Stenosis. David Riesman, Philadelphia.

2. Signs of Persisting Infection in Acute Rheumatic Fever. Clifford L. Derick.

3. Hemorrhagic Nephritis. James P. O'Hare.

4. A Surgeon's Views of the Treatment of Peptic Ulcer. David Cheever.

5. Neurosurgical Conditions. Harvey Cushing.

FRIDAY, APRIL 12, 1929

1. Hypertension. Charles F. Martin, Montreal.

2. Vascular Disease in Diabetes Mellitus. Reginald Fitz.

3. Treatment of Certain Types of Cardiac Arrhythmia. Samuel A. Levine.

4. Treatment of Trifacial Neuralgia. Gilbert Horrax.

5. Diuretics. Henry A. Christian.

L ROBERT BRECK BRIGHAM HOSPITAL

Program in charge of Louis M. Spears
Clinics on Arthritis

M UNITED STATES NAVAL HOSPITAL

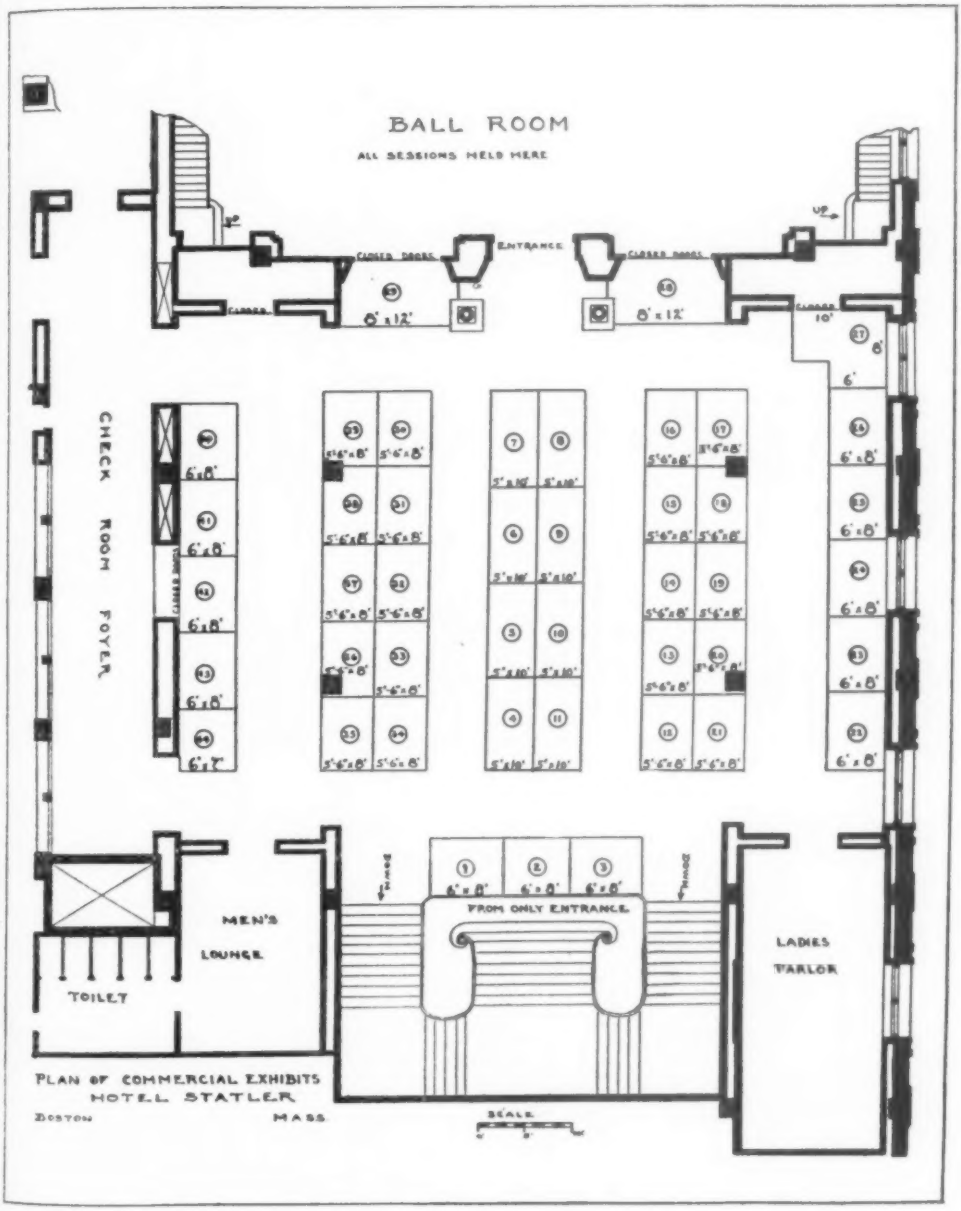
Program in charge of Capt. F. L. Pleadwell, M.C., U. S. N.

Presentation of medical cases in the conference room of the hospital each morning. Following this the group will be split up in sections of five. Each section will be in charge of a ward medical officer, and the balance of the morning will be devoted to ward rounds.

TECHNICAL EXHIBIT

The technical exhibits have been arranged by the Executive Secretary, Mr. E. R. Loveland, and the following chart shows the arrangement of booths and the assignment to exhibitors from various parts of the country. The exhibits are highly diversified in their variety and will bring to the attendants at the Clinical Session, the latest and most improved equipment, the best pharmaceutical products, almost the whole library of medical publications and many other products of special interest to the Internist, Pediatrician, Neurologist, Psychiatrist, Radiologist and research worker.

This Exhibit is undoubtedly the best arranged and the most popular one that The College has yet had. The location is in the Ballroom Foyer where all attendants to the meeting will pass through the exhibits daily. The Joseph T. Griffin Decorating Company, of Louisville, Kentucky, who installed the exhibits for the American Medical Association, the Southern Medical Association and many other prominent medical societies, will be in charge of the booths and decorations.


BALL ROOM
ALL SESSIONS HELD HERE
ENTRANCE
CLOSED DOORS
CLOSED
UP
8' x 12'
CHECK ROOM FOYER
MEN'S LOUNGE
TOILET
FROM ONLY ENTRANCE
LADIES PARLOR
PLAN OF COMMERCIAL EXHIBITS
HOTEL STATLER
BOSTON MASS
SCALE

LIST OF EXHIBITORS

Space	Name	City and State	Product
20	Abbott Laboratories	North Chicago, Ill.	Pharmaceutical Products
12 & 21	D. Appleton & Company	New York, N. Y.	Medical Publications
31	The Battle Creek Food Company	Battle Creek, Mich.	Health Foods
22	Bausch & Lomb Optical Co.	Rochester, N. Y.	Microscopes, Photomicro & Projection Apparatus
40	P. Blakiston's Son & Co.	Philadelphia, Pa.	Medical Publications
13	The Borden Sales Company, Inc.	New York, N. Y.	Merrell Soule Infant Foods
26	Britesun, Inc.	Chicago, Ill.	Therapeutic Lamps
25	Cambridge Instrument Co., Inc.	New York, N. Y.	Electrocardiographs & Accessories, and other Physiological Instruments
3	Cameron's Surgical Specialty Co.	Chicago, Ill.	Electro-Diagnostic Surgical & Dental Instruments
44	G. W. Carnrick Co.	Newark, N. J.	Pharmaceutical Products
1	Warren E. Collins, Inc.	Boston, Mass.	Metabolism and Oxygen
49	Davies, Rose & Co., Ltd.	Boston, Mass.	Trethylene, Pil. Digitalis, Shadocal
14	F. A. Davis Company	Philadelphia, Pa.	Medical Publications
16	Deshell Laboratories, Inc.	Chicago, Ill.	"Petrolagar"
42 & 43	General X-Ray Company	Boston, Mass.	"Morse" Wave Generator, GX-Galvine-Faradie Plate, Diathermy Apparatus, Electrodes
34	Paul B. Hoeber, Inc.	New York, N. Y.	Medical Publications
19	Horlick's Malted Milk Corporation	Racine, Wis.	Malted Milk Products
17	Kalak Water Company, Inc.	New York, N. Y.	Kalak Water
4	Charles B. Knox Gelatine Co., Inc.	Johnstown, N. Y.	Knox Gelatine
15	Lavoris Chemical Company	Minneapolis, Minn.	"Lavoris"
45	LaMotte Chemical Products Co.	Baltimore, Md.	LaMotte Blood Chemistry Outfits
30	Lea & Febiger	Philadelphia, Pa.	Medical Publications
47	Lederle Antitoxin Laboratories	New York, N. Y.	Biological Products and Pharmaceutical Specialties
9	J. B. Lippincott Company	Philadelphia, Pa.	Medical Publications
29	MacGregor Instrument Company	Needham, Mass.	Vim Stainless Steel Needles; Vim Emerald Luer

29	MacGregor Instrument Company	Needham, Mass.	Vim Stainless Steel Needles; Vim Emerald Luer Syringes; Vim Surgical & Medical Specialties
8	The Macmillan Company	New York, N. Y.	Medical Publications
2	E. F. Mahady Company	Boston, Mass.	Anaesthetic Apparatus, Laboratory Equipment, Diagnostic & Scientific Apparatus, Vaccines, Intravenous Products, Orthopedic Appliances & Supplies, Instruments for Operating Room, E.F.M. Catgut
18	The Medical Protective Company	Chicago, Ill.	Malpractice Insurance
24	Mellin's Food Company	Boston, Mass.	Mellin's Food
38	Merck & Company, Inc.	Rahway, N. J.	Pharmaceutical Products
23	The Wm. S. Merrell Company	Cincinnati, Ohio	Pharmaceutical Products
32 & 37	Merrell Soule Company	New York, N. Y.	Infant Foods
35	The C. V. Mosby Company	St. Louis, Mo.	Medical Publications
39	Thomas Nelson & Sons	New York, N. Y.	Medical Publications
28	The E. L. Patch Company	Boston, Mass.	Cod Liver Oil
6	Pittsburgh Plate Glass Co.	Pittsburgh, Pa.	"Helioglass"
7	Richards, Inc.	Glenolden, Pa.	Psyllium Seed & Acidophilus Products
11	W. B. Saunders Company	Philadelphia, Pa.	Medical Publications
27	Sanborn Company	Cambridge, Mass.	"Graphic" Metabolism Apparatus
41	Spencer Lens Company	Boston, Mass.	Optical Instruments, Projection Apparatus, Laboratory Equipment
50	Swan-Myers Co.	Indianapolis, Ind.	Pollens, Ephedrine Preparations, Dextrose Ampoules and other Pharmaceutical Products
36	Tailby-Nason Company	Boston, Mass.	Cod Liver Oil
51	Taylor Instrument Companies	Rochester, N. Y.	"Tycos" Sphygmomanometer, Thermometers and Hygrometers
5 & 10	Victor X-Ray Corporation	Chicago, Ill.	Electrocardiograph & Quartz Lamps
46	Vitaglass Corporation	New York, N. Y.	Vita Glass
33	Winthrop Chemical Company, Inc. H. A. Metz Laboratories, Inc.	New York, N. Y.	Pharmaceutical Products

BAUSCH & LOMB CO.

BOOTH 22

In each issue of this publication for the past few months, this space has been devoted to a brief description of a partial list of the optical instruments which Bausch & Lomb manufacture for the medical Profession.

At the American College of Physicians meeting, April 8-12, 1929, the instruments which have been described herein will be on exhibit. A list of the instruments to be exhibited are:

Microscopes	Hemoglobinometers
Microtomes	Centrifuges
Colorimeters	Haemacytometers

The physician who is contemplating buying new instruments will find this exhibition an excellent place to make his choice. Undoubtedly some who do not intend to purchase will be able to obtain a great deal of useful information on new instruments and improved methods, which should aid them in their practice.

Literature which will give a comprehensive knowledge of the latest developments in the field can be had at the Bausch & Lomb booth. If, however, you do not attend the meeting, the literature will be sent to you upon application to the Company.

P. BLAKISTON'S SON & CO.

BOOTH 40

The translation of Kaufmann's Pathology by Dr. Stanley P. Reimann, published by Blakiston in January, makes available to all American physicians and scientists a work of international repute, whose usefulness has been confined previously to those having a high aptitude for scientific German. The work is a most complete human pathology, general and special. Subjects of most importance to the practicing physician are emphasized and given in great detail. The work is in three volumes and contains 1072 illustrations, those of the last German edition being amplified by many unique pictures drawn by the staff artist at the Lankenau Hospital. A descriptive prospectus will be sent by the publisher upon request.

THE BORDEN SALES COMPANY, INC.

BOOTH 13

In 1856 the first successful process for condensing milk was patented by Gail Borden. Today, 73 years later, the annual world production of all forms of concentrated milk amounts to more than three billion pounds, of which approximately 60 per cent is manufactured in the United States. The Borden Company continues to be the leading producer and distributor of condensed, evaporated, powdered and malted milks, and other milk products.

DESHELL LABORATORIES, INC.

BOOTH 16

Prominent among the exhibits at the next Clinical Session will be Petrolagar—the emulsion of mineral oil.

Samples and literature pertaining to the wide application and usefulness of Petrolagar may be obtained by addressing 536 Lake Shore Drive, Chicago, Illinois.

Dr. F. M. Pottenger (Fellow and Regent), Monrovia, California, and Dr. Egerton Crispin (Fellow and Governor), Los Angeles, California, sponsored a subscription dinner of the Fellows and Associates of The College at the California Club, Los Angeles, on January 18.

The purposes, ideals and future plans of The College were presented, and Dr. Leonard G. Rountree (Fellow), Professor of Medicine at the University of Minnesota and Director of the Medical Service at the Mayo Clinic, delivered an address on "Recent Advances in the Knowledge of the Liver." Such gatherings of members of The College are inspiring and helpful, and it is hoped that groups in other parts of the country will follow this plan of getting together socially and professionally.

Dr. C. W. Stone (Fellow), Cleveland, is President of the Ohio State Medical Association, and will preside at the annual session to be held in Cleveland in May.

Dr. Howard T. Karsner (Fellow), Cleveland, has resumed his activities at the Western Reserve University, following a year's

leave of absence with the National Research Council at Washington.

The summer of 1929 will see the new Institute of Pathology at the University opened. Dr. Karsner will head this Institute.

Dr. Clyde L. Cummer (Fellow), Cleveland, is Councilor for the Fifth District of the Ohio State Medical Association. This year the State Association holds its Convention at Cleveland.

Dr. Morris Weissberg (Fellow), Brooklyn, read a paper entitled "Xanthoma Diabeticorum" on December 12, 1928 before the Brooklyn Medical Association.

Dr. John J. Pflock (Associate), Chicago, has been appointed by Dr. Kegel, Health Commissioner of Chicago, as a member of the Advisory Council Staff of the Chicago Health Department.

At a recent meeting of the Advisory Committee, Dr. Alvah A. Swayze's resignation as head of the Medical Division of the Hackensack Hospital was accepted with regrets. *Dr. Herman Trossbach* of Bogota was appointed to fill the vacancy.

Dr. Elliott B. Edie (Fellow), Uniontown, Pa., was elected Chairman of the Medical Section of the Pennsylvania State Medical Society at its last meeting. The Section officers are responsible for the preperation of the program for the annual meeting, which will be held in Erie, September 30, 1929.

Dr. Edie is in charge of a Heart Clinic, which opened in Uniontown, January 8, 1929, at the suggestion of the Pennsylvania Heart Association. The Pennsylvania State Department of Health will furnish the supplies and nursing service. The Clinic will be open every Tuesday at 11 o'clock in the Red Cross Rooms, Fayette Title & Trust Building.

Dr. John F. Kenney (Associate), Pawtucket, R. I., at the request of the Rhode Island State Welfare Commission recently completed a reorganization of the Laboratory of the State Hospital.

Drs. F. C. Oldenburg (Fellow) and H. V. Paryzek (Fellow), both of Cleveland, were elected to the Board of Directors of the Academy of Medicine of Cleveland at its recent annual meeting. They will serve for a period of three years.

Dr. Oldenburg has been promoted to Senior Clinical Instructor in Medicine at the Western Reserve University Medical School; he is also Secretary and Treasurer of the Western Reserve Medical Alumni Association; and Secretary of the Staff of St. Vincent de Paul Charity Hospital in Cleveland.

Dr. G. T. Harding, Jr. (Fellow), Columbus, Ohio, is President of the Columbus Academy of Medicine for the year 1929.

Dr. J. W. Torbett (Fellow), Marlin, Texas, reports that the Torbett Sanatorium has taken over the Imperial Hotel owned by Dr. J. W. Cook, recently deceased, and combined the institutions all in one known as the "Torbett Sanatorium, Majestic Hotel and Annex." The new institution has 175 beds with all departments in proximity to one another for diagnosis and treatment of all classes of chronic diseases and especially catering to the tourists of the North who come to Texas for the winter. The dining room is under the supervision of an expert dietitian, and ten doctors comprise the staff.

Dr. L. D. Sargent (Fellow), Washington, Pa., has recently returned from a European trip of three months. His time in London and Paris was devoted entirely to the study of diseases of the heart and lungs.

Dr. Robert M. Moore (Fellow), Indianapolis, on January 10 addressed the McLean County Medical Society at Bloomington, Illinois, his subject being "Some Considerations in Heart Failure of the Anginal Type."

Dr. Ray M. Balyeat (Fellow), Oklahoma City, read a paper on "Perennial Hay-Fever" at the Asheville Meeting of the Southern Medical Association, and the discussion was opened by Dr. Grafton Tyler Brown (Fellow), Washington, D. C.

Dr. Howard L. Hull (Fellow), Elma, Washington, was elected President of the Grays Harbor County Medical Society for 1929.

Dr. William J. Mallory (Fellow), Washington, D. C., read a paper on "Diet in Diabetes" before the American Dietetic Association at its meeting in Washington, October 29-31, 1928.

By invitation, he also read a paper before the annual meeting of the Seaboard Medical Association of Virginia and North Carolina, December 4-6, 1928, Washington, N. C., on "The Management of the Complications of Diabetes, Acidosis and Infection." "Gas on the Stomach, a disturbance of Motor Function" was the title of another paper which Dr. Mallory read before the George Washington University Medical Society, recently.

Dr. Wilfred E. Chambers (Fellow), Medical Officer in Charge, U. S. Veterans Hospital, Kansas City, Missouri, addressed the War Mothers of Missouri and Kansas at Memorial Hall, Independence, Mo., October 16, 1928 on the medical care and treatment of the ex-service disabled of the U. S. Military forces.

He also addressed the Gold Star Mothers of Missouri at the Hotel Muelbach, Kansas City, November 13, 1928, on the medical care and treatment of the ex-service of the U. S. Military Forces in foreign countries and disabled ex-service of our Allies in the United States.

On September 20, 1928, Dr. Chambers addressed the Veterans of Foreign Wars at Kansas City on hospitalized patients who had previously fallen into the hands of the charlatan and the evil results thereof, financially, mentally and physically.

An article entitled, "Rehospitalization" by Dr. Chambers, published in the January 1929 issue of the U. S. Veterans Bureau Bulletin, wil be of interest to those concerned directly, or indirectly, with the medical care and treatment of ex-service men of the U. S. Military Forces.

Dr. I. D. Bronfin (Fellow), addressed the Colorado Tuberculosis Association on January the twenty-fifth, 1929, on "Tuberculous Infection and Disease in Childhood" and the Public Health Section of the Colorado State Nurses Association on February the seventh, 1929, on the subject of "Juvenile Tuberculosis."

Dr. Louis O. S. Wallace (Fellow), formerly of Kalamazoo, Michigan, was recently appointed First Assistant Physician on the Medical Staff of the Sonoma State Home at Eldridge, California.

Dr. Wallace has been elected to membership in the American Psycho-Pathological Association and in the American Association for the Advancement of Science.

Dr. Albert B. Yudelson (Associate), Assistant Professor of Neurology, Northwestern University Medical School, Chicago, read a paper entitled "Remission of Tabetic Symptoms Following Sacral Injection of Physiological Solution" on December 20, 1928, before the Chicago Neurological Society. Dr. Yudelson has spent fifteen months investigative work on this subject and uses lantern slides and demonstrates the technique when presenting the paper.

In the Editorial on the Early Manifestation of Leprosy in the November issue of the Annals the Director of the Leprosy Receiving Station in Honolulu should have been given as N. E. Wayson and not J. T. Wayson, who was the former Director of the Station.

OBITUARY

Dr. Eugene Wilson Murray (Fellow, February 8, 1921), Newark, New Jersey, died September 18, 1928, aged 54 years.

Dr. Murray, after graduating from the Northwestern University, School of Pharmacy, attended the Syracuse University, College of Medicine, receiving his medical degree in 1898. He was an interne at the New York City Hospital 1898-99, Attending Physician to the Presbyterian Hospital (Newark) 1913 —, Medical Director of the Newark Babies' Hospital 1916 —. He was a member of the Phi Kappa, Psi Upsilon and the Nu Sigma Nu Fraternities; also a member of his County and State Medical Societies and the American Medical Association.

Dr. John Lincoln Macumber (Fellow, December 27, 1919), Brooklyn, N. Y., died December 22, 1928, of cerebral hemorrhage; aged 67 years.

Dr. Macumber graduated from the Long Island College Hospital, Brooklyn, in 1883, and pursued postgraduate study later at Columbia University College of Physicians and Surgeons and at Fordham University School of Medicine. From 1886 to 1889, he was assistant physician to the Kings County Insane Asylum, and superintendent of the same institution from 1890 to 1891. His more recent appointments were: consulting neurologist, Brooklyn States Hospital, 1900 —; clinical assistant neurologist, Vanderbilt Clinic, 1908 —; attending psychiatrist, Kings County Hospital, 1925 —; clinical instructor, Long Island College Hospital, 1926 —; attending neurologist; Swedish Hospital, 1902 —; attending neurologist, St. Catherine's Hospital, 1913 —; attending neurologist, Lutheran Hospital, 1921 —.

In addition to being a Fellow of the American College of Physicians, Dr. Macumber was a member of his County and State Medical Societies, and a Fellow of the American Medical Association.

Dr. Marinus Larsen Holm (Fellow), Lansing, Mich., died December 24, 1928, of pulmonary tuberculosis; aged 50.

Dr. Holm was born in Denmark in 1878, and came to the United States at an early age. He received his Ph.G. and Ph.C. degrees from the Northwestern University School of Pharmacy, and then completed the medical course in the medical department of the same institution in 1907. He did postgraduate work at Paris and Dijon. From 1902 to 1903 he was instructor in pharmacy at Northwestern University, and assistant in the department of physiological chemistry in the same institution from 1903 to 1906. From 1906 to 1907, he was assistant city chemist, Chicago Department of Health, and from 1907 to 1916, state bacteriologist for the state of Michigan; from 1919 to 1924 he was pathologist of the Sparrow Hospital at Lansing; from 1912 to the time of his death he was a member of the Medical Milk Commission at Lansing, and from 1921 a member

of the Lansing Board of Health. He served during the World War with the successive commissions of Lieutenant, Captain and Major in the Medical Corps of the U. S. Army, and was pathologist with the American Expeditionary Forces.

Dr. Holm was an ex-president of the Ingham County Medical Society, a member of the Michigan State Medical Society and a Fellow of the American Medical Association. He had been a Fellow of the American College of Physicians since 1920.

Dr. Joseph Goldberger (Fellow, March 10, 1923), surgeon, U. S. Public Health Service, Washington, D. C., died January 17, 1929, due to hypernephroma of the left kidney with metastasis in the lung, aged 48 years.

Dr. Goldberger received his medical degree from the Bellevue Hospital Medical College, New York, in 1895; "was commissioned in the public health service in 1899, in which his early assignments were at Tampico, Mexico, in connection with yellow fever, where he contracted the disease. He served also at Ponce, P. R., Vera Cruz, Mexico, in Texas, and during the epidemic of yellow fever in the South in 1905. With the exception of absences due to such investigations as that of dengue fever in the South in 1907, at which time he contracted dengue, and the investigation of straw mite disease in New Jersey, the cause of which he discovered, he had been attached to the Hygienic Laboratory for many years. Other notable investigations were carried on in connection with measles and typhus fever, which he contracted in Mexico City, 1909-10. There he demonstrated that typhus can be transmitted not only by the body louse but by the head louse.

Dr. Goldberger's most important research was on pellagra, beginning in 1913; he was the foremost exponent of the theory that pellagra is a nutritional disease due to unbalanced diet. In this work he performed outstanding research on animals and man, making repeated trips to the South and other parts of the country where pellagra was prevalent. Pellagra had been recognized a hundred years in the Old World but was first recognized in the United States in 1907."

Dr. Goldberger was the author of a great many articles in various medical journals of the country, and had he lived would have delivered an address before the Thirteenth Annual Clinical Session of the American College of Physicians at Boston, April 8-12. He was a member of the District of Columbia Medical Society, the American Medical Association, the American Association for Advancement of Science, the American Association of Pathologists and Bacteriologists and the American Public Health Association, in addition to being a Fellow of the American College of Physicians.

Thirteenth Annual Clinical Session

of the

AMERICAN COLLEGE OF PHYSICIANS

BOSTON, MASS., APRIL 8–12, 1929

The 1929 Clinical Session will constitute one of the most important post-graduate weeks in the history of the College. The Harvard Medical School, the Boston University School of Medicine, Tufts Medical School, Boston City Hospital, Boston Dispensary, Children's Hospital, Homeopathic Hospital, Massachusetts General Hospital, Peter Bent Brigham Hospital, Robert Breck Brigham Hospital, Beth Israel Hospital, New England Baptist Hospital, New England Deaconess Hospital, U. S. Naval Hospital, Carney Hospital and the House of the Good Samaritan are cooperating and arranging programs. Eminent authorities from all parts of the country will participate in clinics, laboratory demonstrations, symposia and formal addresses. *See the College News Notes section for additional details of the program.*

Transportation: Over all railroads of the United States and eastern Canada on the Certificate Plan of reduced fares. Special trains from and to Chicago over the Michigan Central Railroad; special trains from and to Washington over the Pennsylvania Railroad and associated roads. Time-tables for special trains may be secured from ticket offices or passenger agents of roads mentioned, or from the Executive Secretary.

College Smoker, Tuesday evening, April 9; *College Banquet*, Thursday evening, April 11; *Convocation*, for the conferring of Fellowships, Friday evening, April 12.

Headquarters: Hotel Statler. Make reservations immediately.

For Information, address the Executive Secretary.

CHARLES F. MARTIN, M.D., *President*
Montreal, P. Q., Canada

JAMES H. MEANS, M.D., *Chairman*
Boston, Mass.

E. R. LOVELAND, *Executive Secretary*
133-135 South 36th Street, Philadelphia, Pa.